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Book /Report

New Title: REGULATING PESTICIDES

from the Environmental Studies Board, Commission on Natural Resources, National Research Council

Dear Reader,

Recent years have seen a growing public awareness and concern about the untoward effects of widespread pesticide use on the public's health and on ecological conditions. Yet pesticides make a great contribution to our ability to produce food and vegetable fibers, to the amenities afforded by parks and decorative plants, and to the control of pest-borne diseases. Those opposing realities raise complex questions about how to balance the risks and benefits to our society of pesticide use. The problem is immense--over 35,000 pesticides, made up of some 500 active ingredients, must be evaluated to determine their toxicity, risks to public health and the environment, and beneficial impacts in agricultural and other uses.

REGULATING PESTICIDES, a significant new release from the National Academy of Sciences, examines and evaluates the methodology used by the Office of Pesticide Programs (OPP) in the Environmental Protection Agency in reviewing individual pesticides. The report not only develops and recommends more explicit analytical methods for risk and benefit assessments of pesticides but also tests those recommendations in the course of a review of the pesticide chlorobenzilate, chosen as the illustrative example. In its 290 pages, the report

- reviews the legislative and legal status of the Federal Insecticide, Fungicide, and Rodenticide Act of 1947.
- recommends procedures for determining the order in which pesticides are to be considered for further analyses.
- scrutinizes the methods by which risks to public health and the environment and economic benefits are assessed by OPP, with special emphasis on the assessment of carcinogenic risk and the benefits of agricultural pesticide use, and examines the effects of alternative regulations on the risk-benefit assessment.
- considers the generation of alternative regulatory options and the comparison of the effects of the alternative options studied as a function of the administrative decision-making process.
- tests the feasibility of the proposed recommendations during a review of the pesticide chlorobenzilate by the authoring committee.

The contents listing on the reverse of this announcement demonstrates the comprehensive scope of this report.

Significant changes in methodology and procedures are recommended in several areas. Among them are these:

- OPP should assign priorities, as determined by relative toxicity and extent of use, to the 500-odd active ingredients used in registered pesticides; registered pesticides should be considered for in-depth evaluation in the order of the priorities that have

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been assigned to their active ingredients. Potentially hazardous alternative pesticides available for major uses should be reviewed at the same time.
- OPP should abandon attempts to produce numerical estimates of the effects of pesticide use on human mortality and morbidity except when reliable human epidemiological data are available.
- Estimates of risks and benefits, which are subject to substantial ranges of uncertainty, should be expressed as a pair of numbers, one showing the "most-probable" and the other showing the "maximum-plausible" level likely to be experienced.

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Regulating Pesticides

A Report Prepared by the

COMMITTEE ON PROTOTYPE
EXPLICIT ANALYSES FOR PESTICIDES
Environmental Studies Board
Commission on Natural Resources
National Research Council

NATIONAL ACADEMY OF SCIENCES
Washington, D.C. 1980

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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Preface

Recent years have seen a growing public awareness and concern about the effects of widespread pesticide use on public health and on ecological conditions. At the same time it is realized that pesticides make a great contribution to our ability to produce food and vegetable fibers, to the amenities afforded by parks and decorative plants of all sorts, and to the control of pest borne diseases. These opposing realizations have led to our current policy of regulating the use of pesticides so as to permit it when the beneficial effects are deemed to outweigh the hazards, but not otherwise. This policy, in turn, has required the U.S. Environmental Protection Agency to assess the beneficial effects and the risks entailed in the use of specific pesticides in specific circumstances, so as to determine whether regulation was called for and, if so, which specific regulations would service the public best. In 1970, EPA established the Office of Pesticide Programs (OPP) for discharging this responsibility. Ever since then OPP has been developing and applying methods of analysis that would enable it to reach sound and justifiable judgments. Their procedures are still evolving.

The National Research Council's Environmental Studies Board has recently conducted several studies on environmental decision making (*Decision Making for Regulating Chemicals in the Environment* and *Principles for Evaluating Chemicals in the Environment*) and decision making in EPA in particular (*Decision Making in the Environmental Protection Agency* and *Pesticide Decision Making*, Volumes II and VII, respectively, in *Analytical Studies for the U.S. Environmental Protection Agency*). The reports suggest that a methodology that makes explicit the benefits and risks involved can be applied to environmental decision making, although with some difficulties. In the early summer of 1977, therefore, EPA's Office of Research and Development requested that the NRC put their previous recommendations to a practical test and attempt explicit analyses for pesticides that are actually under consideration for registration or reregistration. The Committee on Prototype Explicit Analyses for Pesticides (PEAP) was established in early 1978 by the Environmental Studies Board within the NRC's Commission on Natural Resources to respond to EPA's request.

The Committee was charged originally with implementing three prototype explicit analyses independently of EPA's Office of Pesticide Programs. The Committee soon realized, however, that the study would be substantially more effective if the Committee and OPP worked closely together, with OPP providing data and its analyses and the Committee providing advice and consultation. In this way, the Committee would be aware of the data and resource constraints under which OPP must work and would be in a position to recommend methodologies that could be replicated in the future by EPA without NRC assistance.

Thus, before the Committee first met in April 1978, its charge was revised. The Committee was asked to provide a single report (instead of three) describing the procedures and methods it would recommend to OPP and to include illustrations of the recommendations only where OPP's reports deviated from the recommended methodology. By agreement between EPA and the NRC, the pesticide chlorobenzilate was chosen as the illustrative example.

The study was conducted in two phases: an initial period of observation and self-education followed by the formulation of conclusions and recommendations and their illustration. Between the first meeting in April and its second in September 1978, individual Committee members attended EPA working meetings and met in subgroups to exchange observations and ideas. Committee staff gathered information and briefed the Committee. In August, the Committee divided into risk and benefit subgroups, each to focus on its respective aspect of pesticide assessment.

From September through the end of the study the subgroups met a total of four times and the full Committee met an additional three times to discuss risk and benefit assessment methodologies and the weighing of the two and to develop recommendations to EPA. The Committee's November meeting was held in the citrus-growing region of Texas, so that the Committee could meet with individuals directly involved with chlorobenzilate (a miticide used mainly on citrus).

ACKNOWLEDGMENTS

The nature of this study required exceptional efforts and contributions on the part of the Committee's staff. The staff consisted of Adele King, Principal Staff Officer; Connie Reges, Project Secretary; Russell Settle, Staff Officer; and Lawrence Wallace, Staff Officer. All four were confronted with unexpected responsibilities for contributing to the work of the Committee and discharged them admirably. In fact, in addition to the normal support functions, the staff was called upon to perform most of the research and much of the writing required to prepare our report.

Anonymity should not be preserved in these conditions. The appropriate credits follow.

Chapter 2. Ms. King gathered most of the factual material used in the chapter and wrote about half of it.

Chapter 3. All the factual material was gathered by Ms. King, Dr. Settle, and Mr. Wallace. Ms. King and Dr. Settle collaborated in writing the entire chapter, including the discussion and explanations of the recommendations reached by the Committee. Dr. Settle contributed significantly to the discussion on the role of alternative pesticides.

Chapter 4. The description of the procedures currently followed is the work primarily of Ms. King. Mr. Wallace provided early drafts of the discussion of the methods used to estimate human and other exposures. Much of the responsibility for writing the chapter and for explaining the Committee's recommendations was borne by Ms. King.

Chapter 5. This chapter is essentially the work of Dr. Settle, who both formulated the analysis and prepared the final draft with the benefit (or impediment) of general guidance from members of the Committee.

Chapter 6. The description of the procedures currently followed in OPP was prepared and written by Ms. King and Dr. Settle.

Chapter 7. The test of chlorobenzilate was conducted and written by Ms. King, Dr. Settle, and Mr. Wallace under the general supervision of members of the Committee.

Ms. Connie Reges earned the Committee's gratitude by her cheerful and expeditious discharge of the voluminous paperwork, and by the unconquerable patience she exhibited in communicating with the Committee and in coordinating the numerous drafts of this long report. We also appreciate the assistance from the CNR Editorial Office and the Manuscript Processing Unit.

It might seem from the forgoing that with such a staff the Committee had nothing to do. This was far from the case, and as Chairman I want to record my gratitude for the many hours that the members of the Committee devoted to their tasks, and for their patience in teaching me the many things that the Chairman of such a Committee has to know about matters far removed from his own field of specialization.

The Committee expresses its gratitude to EPA's Office of Pesticide Programs for its generous cooperation. In particular we thank Deputy Assistant Administrator Edwin L. Johnson for his support of the Committee's purpose; Fred Arnold for his willingness to share his knowledge of OPP's Rebuttable Presumption Against Registration (RPAR) procedure; and Kevin Keaney, who attended Committee meetings, kept the Committee current on OPP's activities, and responded patiently to frequent requests from the Committee and staff for documents and data from OPP. Others in EPA's pesticide program and Carcinogen Assessment Group (CAG) gave freely of their time in thoughtful discussion, among them Elizabeth Anderson, Arnold Aspelin, Kyle Barbehenn, Nancy Beach, Joe Boyd, Christen Chaisson, Harold Gaede, Mark Luttner, David Severn, Ellen Siegler, and Bill Waugh. There were many others.

Our special appreciation is due Roy Albert, Chairman of EPA's Cancer Assessment Group; Nathan Karch, Acting Senior Staff for Toxic Substances and Environmental Health for the Council on Environmental Quality; and Umberto Saffiotti, Chief of NCI's Experimental Pathology Laboratory, for their thoughtful discussions with Committee members and their suggestions regarding the Committee's recommended cancer risk assessment methodology. It should be noted that the help of any of the individuals singled out for thanks above does not imply their endorsement of Committee findings.

We also thank Michael Wallace, Executive Vice President of Texas Citrus Mutual, who arranged for the Committee to meet in McAllen, Texas, with entomologists, researchers, growers, market specialists, and others directly involved with the pesticide chlorobenzilate and the Texas citrus industry. Drs. Jon Allen, Robert Brooks, and Joseph Knapp also attended this meeting, in addition to providing other information.

John Krummel searched the literature on biological aspects of chlorobenzilate which provided background for the section in Chapter 7 on yield effects. Bob Bukantis did the same for biological aspects of dimethoate, as presented in Appendix D.

Dr. Alan Carlin, EPA's Project Officer in charge of our contract, attended most of our meetings and contributed valuable insights to our discussion. He was a supportive and understanding colleague throughout this study, even when its focus shifted from the area he originally intended, when the Committee reached conclusions that conflicted with his own convictions, and when the study threatened to continue endlessly in bland disregard of his deadlines. Needless to say, Dr. Carlin bears no responsibility for our findings in spite of his indispensable contributions to our work.

ROBERT DORFMAN, *Chairman*
Committee on Prototype
Explicit Analyses for Pesticides

1 Summary and Major Recommendations

INTRODUCTION

This report is an outgrowth of the work of the NRC's Committee on Environmental Decision Making (CEDM). The first recommendation in that Committee's report reads as follows (NRC 1977c:10):

> EPA's decisions on standards and regulations should be supported by analyses that explicitly state the objectives of the decisions, identify feasible alternatives, evaluate (quantitatively, to the extent possible) the consequences of each alternative decision, explore potential problems in implementation, and indicate and examine the degree of uncertainty about the effects of EPA actions. The analyses should be available to the public.

The authors of that recommendation knew they were setting forth an ideal that many branches of EPA were already striving to attain, and that there was much doubt within EPA that it was feasible to come noticeably closer to attaining that ideal than already was the case, in view of the limited resources and information available to the Agency. The CEDM, however, did not share those doubts. On the contrary, it felt that by intelligent use of the available information and resources EPA could implement the recommendations far more consistently than it had been doing. The CEDM made extensive suggestions to this effect (NRC 1977c:25–36).

With this background, EPA entered into a contract in late 1977 under which the National Academy of Sciences would study the feasibility of implementing routinely the quoted recommendation. This was to be accomplished by the most practical test of actually undertaking to assess the risks and benefits of three pesticides. The Committee on Prototype Explicit Analyses for Pesticides (PEAP), appointed to undertake these three assessments, soon requested that its charge be revised to provide for a closer direct involvement with EPA's Office of Pesticide Programs (OPP). The new charge to the PEAP Committee was to observe OPP's assessment of three pesticides and to provide advice and consultation directly to OPP on how to make its analytical assessment methodology more explicit. The methodological recommendations developed from this experience would be written up as the Committee's report and illustrated, to the extent that OPP's three assessments did not follow the recommendations, using the three pesticides OPP was assessing. The focus of the Committee's study was to be OPP's mechanism for conducting benefit-risk analyses, the Rebuttable Presumption Against Registration (RPAR) process.

Shortly after beginning to work with OPP, the Committee recognized the overwhelming problem that confronted OPP and its attendant delays. Chapter 3 describes how OPP is charged with issuing literally thousands of legally defensible regulations each year concerning the use of pesticides in U.S. agriculture and elsewhere. The critical need that preoccupies OPP is for procedures and methods that will enable it to process as rapidly as possible the thousands of decisions it is required to make. As soon as PEAP became aware of this urgent need, it tried to meet it.

This report is the Committee's attempt. The Committee has not ignored its charge to develop and implement more explicit analytical methods for risk and benefit assessments, but it has embedded that charge in the larger and more immediate problem. In order to expedite its work, the Committee has concentrated on a single pesticide, chlorobenzilate, instead of three.

Chapter 2 reviews the legislative and legal status of the Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (FIFRA) as amended, which is the legal foundation of OPP's activities. The chapter also describes the administrative procedures that OPP has devised to carry out its responsibilities under the Act.

The subsequent chapters discuss in more detail the procedures used by OPP, together with recommended changes the Committee believes will enable OPP to perform analyses in accordance with the recommendation of the CEDM and to do so expeditiously and within the severe constraints of resources and information available to OPP.

Chapter 3 deals with a problem of broad strategy: the determination of the order in which pesticides are to be considered for further analyses and possible regulation. As the Committee sees it, the judicious ordering of tasks is the key to the fulfillment of OPP's responsibilities.

Chapters 4 and 5 deal with a pair of parallel tasks that have to be performed for each pesticide considered. Chapter 4 is concerned with assessing the risks to public health and to the environment that result from the use of a pesticide and with the effects of alternative regulations on those risks. Chapter 5 deals with the parallel assessment of the social and economic benefits of the use of a pesticide and, again, of the changes in those benefits that result from various regulatory alternatives.

Chapter 6 seeks to bring those two assessments together. This is, perhaps, the most difficult part of the task and the part where careful scientific staff work is of least avail. The risks of pesticide use include increases in mortality and morbidity and impairment of environmental vitality and amenities of all kinds. The benefits are largely, but not entirely, an increase in the availability of foods and natural fibers and a reduction in the amounts of resources needed to produce them. It is the responsibility of EPA's Administrator to select the regulatory alternatives for each pesticide that, in his or her judgment, permit the freest possible use of the pesticide that does not impose additional risks that are excessive in relation to the additional benefits they afford. No one can relieve the Administrator of this responsibility. The benefits, for the most part, are the monetary equivalent of economic resources; the risks concern depends partly on the Administrator's personal scale of values and partly on his or her perception of the values held by the society in whose behalf he or she acts. That is to say, it is partly a moral and partly a political judgment. In these circumstances the most that staff and consultants can do is prepare for the Administrator their best reasoned judgment of the material consequences, in terms of all likely benefits and risks, that are apt to follow from any of the alternatives.

The difficulties are magnified by the circumstance that no one knows, or should pretend to know, precisely what risks and benefits will flow from any of the alternatives. The staff has to present to the Administrator its reasoned judgment of the limits within which the risks and benefits of the various alternatives are likely to lie. Frequently these will be very broad limits, in spite of the best efforts of the staff to narrow them. The Administrator's task is then more difficult, but it would be misleading for the staff to convey an impression of more certainty than its knowledge affords. The final chapter, Chapter 7, is a sample application of the methods recommended by the Committee in the chapters that precede it.

Although the entire study was conducted within the context of OPP, the Committee did not lose sight of its broader objective: to study empirically the feasibility of implementing CEDM's recommendation that the benefits and costs of environmental regulations be assessed by explicit and quantitative (insofar as possible) evaluation. The Committee concluded that a policy of maximum explicitness and quantification would facilitate the work of OPP by enforcing systematization and standardization and by increasing the clarity of communication among the various specialists and levels of authority involved. The Committee believes that this conclusion, as well as many of the detailed recommendations listed below, is applicable with equal force to other branches of EPA, and it hopes that its recommendations will be accepted in that light.

In one important respect, however, the Committee found that OPP was already carrying quantification to an unwarranted extreme. In many of its evaluations OPP attempts to estimate the effects of various potential regulations on human morbidity and mortality. As set forth in detail in Chapter 4, this effort generally places more weight on our understanding of the pathological effects of pesticides than it will bear.

It should be stated before setting forth our recommendations that this Committee, like OPP, labored under severe constraints of resources, time, and talent. There are many issues we have not been able to pursue or to probe as deeply as we should have. We are painfully aware of many deficiencies and gaps in the report. For example, the Committee did not have the time to consider the question of getting much more reliable data (as would be highly desirable) or other questions such as the consideration of biological alternatives to pesticide control. Further discussion of how the scope of this report was limited appears at the end of this chapter. Like OPP, we have done the best we could with the limited resources available.

SUMMARY AND MAJOR RECOMMENDATIONS

Principal recommendations are summarized and discussed briefly below.

CHAPTER 3

With responsibility for regulating some 35,000 pesticides and an analytic staff that, though large in absolute terms, is a small fraction of what is required for the task, OPP is in urgent need of a plan of operation that will direct its attention at the earliest possible time to the pesticides whose uses present the gravest threats to public health and the environment. This plan should be adapted to the fragmentary information now available, should not impose additional burdens on the already overburdened staff, should provide for acquiring all the information that is likely to be available in time to be used in reaching the decisions that require it, and should be flexible enough to be amended as new data emerge. The Committee's recommendations, outlined below, are designed to meet these criteria. The recommendations are closely allied to the concept of generic chemical reviews (U.S. EPA 1978), and like that concept take advantage of the fact that the enormous variety of pesticide formulations makes use of a much smaller number—approximately 500—of active ingredients.

The Committee's first recommendation concerns the all-important matter of deciding on the order in which pesticides should be considered for possible RPAR proceedings. We recommend the following procedure:

- OPP *should review the 500-odd active ingredients used in registered pesticides and identify the ones that appear to be significantly toxic and in widespread use, on the basis of readily available information. Priorities should be assigned to these active ingredients, determined by relative toxicity and extent of use, and* OPP *should consider registered pesticides for* RPAR *proceedings in the order of the priorities that have been assigned to their active ingredients. Pesticide formulations that have the same active ingredients (or ingredients of equal toxicity) should be considered for* RPAR *in an order that reflects the extent to which each formulation is used. The review and preliminary ordering of the 500-odd active ingredients could be done by a committee of consultants.*

This recommendation is discussed in more detail and suggestions for implementing it are made in Chapter 3.

In one important respect, however, it will frequently be necessary to diverge from the priority order established by the procedure recommended above. Particularly during the early stages of the process, some of the information needed to evaluate regulatory alternatives will not be at hand when needed by the RPAR assessment team unless special efforts are made to obtain it. The data in question relate to the public health, environmental, and economic effects of the alternative pesticides that will be brought into use by a regulation that restricts the use of a pesticide high on the priority list. When the alternatives to a pesticide for a particular use are significantly toxic and have not yet been evaluated, assessment of potential regulation requires that their effects be known, in order to estimate the changes in risks and benefits that would result from adopting the regulation. The following recommendation is intended to assure that this information will be at hand at the time that the regulatory decision has to be made.

- *At an early stage of the work of reviewing a pesticide for possible regulation, the pesticides that are alternatives to it in its major uses should be identified. If any of them are presumed a potential toxic hazard and have not* *yet already been reviewed, they should be promoted from their assigned places in the queue and reviewed as promptly as possible.*

One consequence of this recommendation will be that the several pesticides that are alternatives for the same use will be reviewed simultaneously. This will make it possible, and advisable, to issue or deny reregistrations for that use for that group of pesticides, without waiting for decisions on the other uses of many of those formulations. The application of this recommendation also is discussed in detail in Chapter 3.

CHAPTER 4

The use of a pesticide may entail manifold risks. Risks to public health are currently EPA's predominant concern. These include the risks of inducing cancers, mutations, spontaneous abortions, or abnormal offspring. A wide variety of other chronic and acute toxic effects may also be induced. In addition to impairing public health, a pesticide may have adverse effects on nontarget animals and plants, including crops, livestock, and important wild species. Since the purpose of any regulation is to reduce some or all of these risks, estimates have to be made of the severity of the risks under the regulatory options that are considered.

Since risks to public health are currently EPA's primary focus, the Committee concentrated its attention on them, and among these risks paid particular attention to assessing the risks of inducing cancers. It should be pointed out, however, that long-term effects of pesticides on the environment *per se* and eventual indirect effects on humans may, in the long run, be more important than evaluations of risks and benefits based solely on toxicity to animal or human. This report admittedly does not address this important topic.

The Committee scrutinized carefully the methods used by OPP and EPA's Carcinogen Assessment Group. As a result of this scrutiny it came to the conclusion, very much in line with the position of the Director of the NCI (Carter 1979), that our present understanding of the mechanisms of cancer development does not permit us to draw reliable numerical inferences from the kind of laboratory data normally available about the effects of pesticides and other compounds on the development of cancers in humans. The bases for this conclusion are already well known and are set forth at some length in Chapter 4 and Appendix A. On the basis of this conclusion and the fact that, once outside CAG, numerical estimates of human cancer incidences are often misued in EPA's decision making, the Committee makes the following recommendation:

- OPP *should abandon its attempts to produce numerical estimates of the effects of the use of pesticides on human mortality and morbidity except when reliable human epidemiological data are available. In the usual case, in which major reliance has to be placed on the results of bioassays, those results should be used to construct indicators of the relative pathological activity of the pesticide under review in comparison with other pesticides and compounds. The effect on public health of alternative regulations should be presented in the form of estimates of the doses of that pesticide to which pertinent segments of the population will be exposed under those regulations. The doses received should be evaluated according to the pesticide's virulence relative to other pesticides and compounds.*

The Committee recognizes that this recommendation is inconsistent with the practice and methodological recommendations of some previous NRC reports that have, in fact, recommended and used extrapolation techniques to derive numerical estimates of human cancer incidence from animal data (NRC 1972; 1976; 1977a, b, d; 1978a, b). But, for the reasons discussed in this report, the Committee feels that the change suggested here will improve the decision-making process.

The situation with respect to other aspects of public health appears much the same. Empirical data on the mutagenic, teratogenic, and toxic effects of pesticides on human populations are rarely available, and the basis for inferring those effects from laboratory experiments with animals is generally lacking. Consequently, for those hazards also, to the extent that they have to be inferred from laboratory experiments with animals, the Committee recommends that the laboratory data be used to show how the pathological activity of the pesticide under review compares with the activities of other pesticides and compounds in producing effects. The effect on public health can be indicated by estimating the doses to which pertinent segments of the population would be exposed under alternative regulations, taking relative pathological activity into account.

An important component of assessing the effects on public health of using a pesticide is the task of estimating the number of people who would be exposed to it and the doses that major segments of the population would be likely to receive. Empirical data are often deficient or entirely lacking, so that estimates must be inferred from fragmentary sources or by analogy with other pesticides or experiences. Making these inferences requires close familiarity with the conditions under which the pesticide is used and with its routes of transmission, a familiarity that the OPP staff cannot be expected to have in all instances. In order to enhance the quality and reliability of these estimates the Committee makes the following recommendation:

- *It should be a routine practice for the members of the* EPA *staff team reviewing a pesticide to visit sites where it is applied, facilities where it is formulated and handled, and laboratories where it is studied, and on those visits to hold informal discussions with the people in day-to-day contact with the manufacture, handling, and use of the pesticide.*

The risks attendant on the use of a pesticide, as well as the economic benefits that it produces, depend on the length of time it is used. Experience indicates that the economic lives of most pesticides are limited, both because target species frequently adapt to them and because they are often superseded by improved compounds. Unfortunately there is very little information about the economic lives of pesticides or about the factors that influence them. Accordingly the Committee recommends that:

- OPP *should undertake or sponsor a study of the economic lives of pesticides and the factors that influence the economic lifetimes. Estimates of both lifetime exposures and economic benefits should be based on the periods of use that are revealed to be reasonable by this study.*

This discussion and the Committee's investigation generally have revealed that every component of the appraisal of risks is subject to substantial uncertainty. OPP, however, almost always presents its exposure estimates as single figures without an accompanying indication of the degree of uncertainty. Every reader of the estimates, undoubtedly, is aware that the estimates are subject to error, but normally readers have no grounds for judging how large the errors are likely to be. It is important that this information be provided. The format preferred by the Committee is to present two estimates of every component of risk and the data used in deriving those estimates. One of these figures should convey the analyst's best judgment of the level that actually would be realized under the assumed conditions. The other figure should present an estimate of the maximum risk likely to be experienced (barring an extremely implausible chain of unfavorable circumstances). These two estimates are referred to in the text as the "most-probable" and "maximum-plausible" estimates of risk. In the Committee's own work the most-probable estimates correspond generally to the mode in statistical terminology, and the maximum-plausible estimates to the upper limit of a 90 percent confidence interval.

These considerations lead to the following recommendation:

- *The methods now used by* OPP *for estimating the exposures associated with various regulatory options are sensible and, with the modifications discussed above, are as sound and reliable as the available data permit. The resultant estimates, however, are subject to substantial ranges of uncertainty that should always be kept in mind. To this end, estimates that are subject to* *uncertainty should always be presented as a pair of numbers, one showing the exposure or other aspects of risk deemed most probable, and the other showing the maximum exposure or component of risk likely to be experienced (in the absence of an implausible array of untoward circumstances).*

These conclusions, particularly the recognition that unless there are adequate epidemiological data no numerical estimate should be made of the effect of various regulatory options on human morbidity and mortality, have profound implications for the assessment of regulatory alternatives. They imply, in particular, that regulatory decisions have to be made on the basis of data that do not show explicitly the effect of alternative regulations on the attainment of the purposes being pursued. Put differently, it would be far easier to choose among regulations about which the effects on mortality rates or on the rate of incidences of cancers are known than among regulations about which the only available information concerning risks is the estimated doses of chemicals having roughly estimated pathological activities to which populations will be exposed. Yet these are the only data that can be provided to the regulatory authorities in most instances. Chapter 6 discusses at some length the problem of reaching regulatory decisions under these circumstances.

CHAPTER 5

Pesticides confer many kinds of benefits. They are an essential ingredient of modern commercial agriculture and forestry. They contribute to public health by controlling insect vectors of disease. They protect ornamental trees, lawns, and shrubs. They reduce the numbers of insects in residences and other structures. Since, however, the Committee's resources were limited and according to the 1978 estimates (U.S. EPA 1979) about three fourths of all pesticides by volume are used in agriculture, the Committee devoted its review of benefit estimation entirely to agricultural use. In the course of its review, the Committee studied numerous directives and memoranda that prescribe the methods used for benefit evaluation in OPP and evaluated in detail the benefit analyses of six pesticides.

OPP's analyses of the benefits of pesticide use in agriculture are all based on a procedure called "partial farm budgeting." This procedure amounts to estimating the effects of alternative regulations of the use of a pesticide on the net farm incomes of growers of the crop that the pesticide is used to protect. It therefore implicitly defines the economic effect of regulating a pesticide to be its effect on net farm income. But

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effects on the environment." The phrase "unreasonable adverse effects on the environment" is defined in Section 2(bb) as "any unreasonable risk to man or the environment, *taking into account the economic, social, and environmental costs and benefits of the use of any pesticide*" (emphasis added). The standard, "unreasonable adverse effects on the environment," controls the Agency's determinations about the acceptability of a proposed use of a pesticide. A reading of the legislative history supports the Agency's position that FIFRA, as amended by FEPCA, requires the Agency to subject all pesticide uses to benefit-cost (or benefit-risk) analysis. The legislative history is equally clear that in all stages of decision making the analysis should be a balanced one, that is, that equal weight be given to benefits and risks. Congress recognized that some risks are inherent and unavoidable in pesticide decision making, but wanted risks to be weighed against benefits in every decision. Some environmentalists have questioned this reading of the legislative history. They argue, on the basis of drafts and explanations by the environmentally oriented Senate Commerce Committee, that a substantial showing of benefits would be required if a finding of risk were made. However, a close reading of the legislative history indicates that the analysis was to be a balanced one. The "spirit" of the section was summed up by the report of the House Committee on Agriculture, whose version became the final bill: "As the committee labored through the months of hearings and discussions, one central legislative philosophy developed . . . the theme of the 'search of balance!'" (U.S. Congress, House 1971:5).

Any doubts that Congress intended a balanced assessment of benefits and risks were dispelled in 1975 and 1978 amendments to the legislation. A constant theme in the 1975 hearings was that EPA was not giving adequate attention to agricultural development (i.e., benefits of pesticide use) in its decisions. Congress redressed the imbalance indirectly by strengthening the role of the USDA in the decision-making process and by creating a new Scientific Advisory Panel, composed of seven persons appointed from a list of six nominated by the National Institutes of Health and six nominated by the National Science Foundation.

The 1975 amendments have been described as a shotgun wedding between EPA and the USDA. Specifically, FEPCA was amended to require the Administrator of EPA to take into account the effects of cancellation and suspension of a pesticide's use upon the production and prices of the relevant agricultural commodities when the Agency issues a notice of intent to cancel. Further, in connection with final action, the Administrator must prepare and publish an agricultural economic impact statement. To ensure that the Administrator receives the views of the agricultural community, proposed cancellation and suspension notices must be sent this can be misleading. If a regulation increases the cost of producing a certain crop, the total output of that crop will be reduced and its price will generally rise. This rise in price will offset the increase in farm production costs and the decrease in farm revenues caused by the reduction in the size of the crop. The offset can be substantial; in fact, in several of the analyses the Committee studied, it was so great that net farm income was increased as a result of restrictions on the use of a pesticide. But of course national income is not increased. The rise in price that cushions the effects on the incomes of farmers is borne by the consumer, and in a more complete accounting of the effects of the regulation, the loss on the part of consumers would offset completely the cushioning effect of the price rise on the incomes of farmers. The Committee therefore recommends:

- *In applying the partial farm budgeting approach to estimating the benefits of pesticide use,* OPP *should exclude the effects on net farm income of changes in crop prices induced by the regulations.*

A budgeting procedure that implements this recommendation is described in Chapter 5. The estimates obtained by following the corrected farm budgeting approach will be tolerable approximations to the effects of regulations on national income, but they will not reveal the differential effects on farmers, on consumers, and on other population groups whose welfare may be of interest. Those differential effects are often significant. OPP should therefore continue to use its present methods for estimating effects on farm income and should supplement those estimates with estimates of the effects of regulations on the incomes of other population groups. A format for incorporating all these consequences of regulation is also suggested in Chapter 5.

One of the serious problems inherent in estimating the economic effects of regulating pesticides is the difficulty of foreseeing how farmers will respond to regulations, in particular of foreseeing what alternative methods of pest control they will employ. The analytical methods currently used by OPP do not allow for farmers' responses to the differing costs of various methods of pest control nor do they take into account the extent of farmers' experience with different methods. It appears that the mechanical method currently used has a tendency to overstate the loss in benefits that would result from restricting the use of pesticides. Though any forecast of changes in pesticide control methods must be conjectural, the Committee recommends that a more realistic and less biased method be used; one such method is suggested in Chapter 5. In making forecasts it is essential to assemble and evaluate all possible information. The site visits recommended in Chapter 4 will be useful for this purpose.

Under the best of circumstances the estimation of the economic effects of regulating a pesticide is a difficult task. It must employ data from many sources, often unpublished and sometimes very informal. It requires the exercise of considerable judgment in choosing underlying assumptions and in making approximations where data are deficient. For these reasons the resultant estimates require very careful review with respect both to the quality and reliability of the data employed and to the appropriateness and adequacy of the methods used. The current procedures in OPP provide for a highly qualified review of risk assessments (by the Science Advisory Panel) but not for a comparable review of benefit assessments. The Committee therefore places particular emphasis on the following recommendation:

- OPP *should establish an external Benefits Review Panel, similar in organization to the Scientific Advisory Panel, consisting of entomologists, plant pathologists, weed specialists, economists, and others with expertise in assessing the benefits of pesticide use. This panel should have the responsibility of providing external scientific reviews of the benefits data and analyses. For each* RPAR *compound, a review team (consisting, for example, of one entomologist and one economist) should be selected from the panel. This team, in contrast to current* SAP *procedures, should be involved from the earliest stages of the benefits assessment, and should have the primary responsibility for presenting an evaluation of the benefits assessment to the entire Benefits Review Panel.*

CHAPTER 6

Chapter 6 deals with the assimilation of the results of the risk and benefit analyses discussed in the preceding two chapters. It considers two principal topics: the generation of alternative regulatory options and the comparison of the effects of the alternative options studied.

Actually, the generation of the regulatory options cannot wait until the late stages of the study. At least a general preview of the possibilities that eventually will be evaluated is needed from the very inception of the analytic work in order to initiate the accumulation of relevant data and to establish the assumptions to be used in preparing the estimates of risks and benefits. Additional regulatory possibilities are likely to emerge, however, as the work progresses. The plans for analysis should be revised as such new possibilities come to light, so that the data necessary for appraising them will be available when needed.

The options available for regulating a pesticide are generally fairly well standardized. An agricultural pesticide being reviewed for reregistration will normally be used on several crops (food and fiber production accounts for almost 75 percent of pesticide use by volume), in several sections of the country, and for contending with a number of different pests. The regulatory options, then, are choices among which of these uses (if any) are to be allowed and disallowed. Restrictions may also be placed on the mode of application of the pesticide in any or all of the uses and on precautions that may be required to reduce the exposures of people and of nontarget species in general. Considerable familiarity with the pesticide and its use, as well as some exercise of ingenuity, is required to select a manageably small number of significant regulatory alternatives that have good promise of reducing undesirable exposures without imposing prohibitive or excessive costs on the users. It is generally not feasible to analyze more than a half dozen or so alternative options with any thoroughness. The development of alternative options is therefore an important matter, and deserving of considerable deliberation and attention, because it delimits the range of choice. The eventual decision will be a choice of the best of the regulatory alternatives subjected to analysis; regulatory possibilities that may be substantially superior are forever ruled out if they are not included in the list of options subjected to analysis. Thus, the development of the list of regulatory alternatives amounts to a rejection of all possibilities not included in the list and as such is a genuine regulatory decision. It should not be regarded as merely a preliminary stage in the analysis.

The second stage in the decision process is the adoption of one of the options that have been proposed and analyzed. The data pertinent to this choice are the costs of the different options (discussed in Chapter 5 as forgone benefits) and their effect on risks of various sorts (discussed in Chapter 4), all of which are imperfectly known. Furthermore, these costs and risks have to be known or estimated in some detail, since different segments of the population will fare differently under the different options. It cannot be expected that there will be any option that is superior to all the rest from all points of view or from the standpoint of all members of the population. Thus the choice inevitably amounts to choosing among risks of various sorts, between risks and economic costs, and among options that are favorable to different segments of the population. These choices are difficult and cannot be made mechanically.

Choices of this sort are the subject of decision theory, which by now has developed a substantial body of techniques for facilitating decisions. Most of the techniques used in decision theory depend upon the decision maker's "utility function," which is essentially a scale for measuring the relative desirability in his or her esteem of different combinations of costs, risks, and other consequences that may be expected to result from the selection of any one of the options. In the Committee's judgment these utility functions cannot be ascertained in the circumstances in which OPP operates. We therefore recommend procedures that do not employ this concept, but rather consist of presenting in intelligible form a menu or range of choices open to the decision maker. The recommended procedures are discussed in some detail in Chapter 6.

CHAPTER 7

The Committee's work had both a normative and a descriptive aspect. The normative aspect was to make recommendations that would facilitate the analytic and decision-making work of OPP and would increase the cogency of their analyses. The descriptive or empirical aspect was to test the feasibility of those recommendations in the light of the limitations of data, time, and facilities that constrain OPP in reaching its numerous decisions. In the nature of the case, we were not able to formulate a test with any pretentions to scientific rigor. Our test consisted of working through a single decision problem—the choice among alternatives for regulating the pesticide chlorobenzilate—using only data and methods that are available to OPP. We were not able to do even this task completely realistically, because our staff and other resources were far smaller than those that OPP can bring to bear on a similar problem and because we were restricted to using, with some minor exceptions, only the data that OPP had generated in its analysis of chlorobenzilate—although our recommendations called for acquiring certain additional data at an early stage in the study of a pesticide.

Chapter 7 reports the results of this test application of our recommended procedures. We studied five regulatory options and obtained clear indications of their relative merits and demerits. We deliberately refrained from choosing among those options, since the limitations under which we worked made it presumptuous for us to offer such a decision, and since it was not part of our purpose or charge to second-guess OPP's choice. Nevertheless, this small test persuades us that it is entirely practicable for OPP to carry out analyses in accordance with the procedures that we recommend. It is for the reader to judge whether the information yielded by our recommended procedures is significantly more helpful in arriving at decisions than the information provided by OPP's current methods. The Committee thinks that it is.

CONCLUDING REMARKS

The Committee's thinking evolved strikingly in the course of its work. In the beginning, it perceived its task as testing the feasibility of employing the established methods of benefit-risk analysis in decision-making procedures of EPA, using the Office of Pesticide Programs as a test case. Almost immediately it became embroiled in the overwhelming problems that OPP confronts: the problem of processing the reregistrations of some 35,000 pesticides within the tight timetable prescribed by the legislation. The Committee became increasingly impressed by the enormousness of the task assigned to OPP. On the one hand, it was obvious that simple expeditious procedures were required for processing the individual pesticides. On the other hand, it was just as obvious that rough and ready methods would not suffice. The implications of the decisions for public health and environmental integrity were too great, and the stakes that many people had in them were too high for decisions to be reached lightly or without thorough analysis of their implications for consumers, for farmers, for farm workers, and for everyone concerned with health and with environmental conditions.

The recommendations summarized above show that the Committee did not choose to sit on either horn of this dilemma. Life for OPP cannot be made simple, and the Committee quickly abandoned the attempt to make it so. Most of the recommendations are directed to increasing the logical and scientific probity of OPP's analyses. The Committee believes that by following standardized procedures of greater logical clarity, OPP can save some time and effort in the performance of its tasks, but not very much. More time can be saved, and effectiveness can be increased, by following a more systematic strategy for selecting pesticides for review, as recommended in Chapter 3. These improvements can alleviate OPP's predicament somewhat, but they can by no means enable OPP to complete its assigned task within the time allotted. The Committee cannot claim to be offering OPP a solution to its central problem, that of arriving at considered judgments about the regulation of all the pesticides used in this country in a short space of time.

So much for the quantity of decisions. Quality is also important, and here the Committee feels more content with its work. The Committee was impressed by the carefulness and thoughtfulness of OPP's work, but it did observe a number of significant shortcomings. These have already been summarized and there is no need to repeat them. Still it is worth repeating that many of the deficiencies result from inadequacy of the data available to OPP. Insufficiency of data is a frustrating and time consuming obstacle to every phase of the analyses. Appraisals of risk to human health are made complicated and uncertain by the lack of information about human exposures. Estimates of the costs of restrictive regulations are made vague and controversial by the paucity of information about the effectiveness of pesticides. There is little reliable information about the effects of most pesticides on nontarget species of animals or vegetation, wild or domestic. As exemplified in Chapter 7, much of the analytic effort of OPP is devoted to attempting to bridge these gaps in the data by interpolating, extrapolating, or inferring from whatever tangentially relevant information can be found. Research designed to remedy these deficiencies would expedite and strengthen OPP's analyses greatly. Of course, much such research is in progress; it should be pursued vigorously. More complete and systematic monitoring of exposures of people and wildlife to pesticides, and the consequences, are of particular importance.

The recommendations in Chapter 4 concerning the characterization of the pathological potencies of different pesticides point to an area of special concern. This report has already raised strong objections to the methods currently in use. The proposed alternative, Carcinogenic Activity Indicators, have more scientific justification, but they, too, rest on assumptions that stand in need of verification. The CAI's also are somewhat difficult to interpret, though this difficulty may stem largely from their unfamiliarity. Although the Committee recommends that CAI's be employed as indicators of the relative hazardousness of different chemicals, it does not feel that the measure recommended is the ultimate word. Serious research should be undertaken into methods for measuring and expressing the potencies of different chemicals in inducing cancers and other diseases.

This report has commented several times on the vast scope of OPP's task. The Committee's task was correspondingly large, so that we were forced to concentrate on a few salient aspects of the work to the neglect of many other important issues. For example, our review of the analysis of the cost of pesticide regulation was confined to the costs of regulating pesticide use in commercial agriculture. Other uses, for the control of disease vectors, for noncommercial gardening, and many other purposes are by no means negligible, and in fact account for over a third of total pesticide use. Though the Committee could not review the costs of regulating any application of pesticides other than in commercial agriculture, those costs are undoubtedly substantial and the methods used to estimate them should be audited carefully by some specialists who are independent of EPA.

The Committee's review of the estimation of the risks of using pesticides was similarly incomplete. It was limited almost entirely to the estimation of risks to public health, and within that area to the risks of increasing the incidence of cancer and adverse mutations. The Committee feels that most of the risks to public health that result from prolonged exposures to pesticides give rise to issues similar to the ones studied and should be dealt with by similar methods. The estimation of the risks of acute toxic effects is an entirely different, but apparently less difficult, task. The Committee did not consider it. Neither was it able to consider the appraisal of the environmental and ecological consequences of pesticide use beyond noticing that the data available for making such estimates are particularly inadequate and untrustworthy. No attention could be paid to the possibility of long-run climatological, ecological, or evolutionary effects. In short, there are wide gaps in this study, long though it is, gaps that may be serious and which ought to be filled.

Finally, while enumerating the inadequacies that the Committee is painfully aware of, the length of the report has to be included. The report is far too long, but to quote Sam Johnson, "there was no time to make it shorter."

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2 FIFRA and the RPAR Process

LEGISLATIVE FRAMEWORK

INTRODUCTION

The stakes are high in pesticide regulation. The increased yield and subsequent economic return to U.S. agriculture from pesticide technology and the return to the chemical industry have encouraged many to rely on pesticides as a primary means of pest control. Farmers spend more than $2.2 billion a year on chemical pest control, thereby increasing the value of their output by an estimated $8.7 billion, that is, by about 9 percent (Pimentel *et al.* 1978). However, the possibility of substantial risks to human health and to ecosystems from wide-scale use and, sometimes, misuse of chemicals may entail costs beyond those that society is willing to accept. On the other hand, depriving agriculture of an important tool for which there is no substitute may involve risks and economic costs both to the industry and to society that are also unacceptable.

Pesticides, depending upon the dose or exposure level, may produce acute or chronic toxic effects in nontarget organisms, including humans. There is increasing evidence that some chemical pesticides pose long-term cancer and other risks to humans exposed to them through dermal contact, inhalation, or the food chain. Society thus must decide how much, what kinds, and what uses of chemical pesticides to allow.

In recent years, the historical presumption that unrestrained technology is beneficial (the protechnical attitude) has been questioned. Evidence is accumulating, largely from the sciences of public health, ecology, and economics, that technologies may have hidden impacts that produce unacceptable side effects. Consequently, society has increasingly come to accept the proposition that technologies that affect the environment should be rigorously assessed before they are applied.

The case for evaluating technologies by some form of benefit-cost analysis (the analytical attitude) is a strong one, in the abstract. In practice, however, because of the great uncertainties involved in pesticide assessment, rigorous benefit-cost analysis is almost impossible. The most rational comparison of the benefits of using a pesticide with the risks it entails is fraught with uncertainty. Beyond that, stating the question as one of comparing risks against benefits runs the danger of weighting the answer on the side of risks, for there is a general reluctance to balance risks to human health against mere economic gains. Calabresi and Bobbitt (1978) in their book, *Tragic Choices*, explain why society is reluctant to attempt rational trade-offs:

> When tragic choices are made through the pure market within an existing distribution of wealth, costs arise which are external to the immediate decision makers and are borne instead by the rest of us. These external costs may limit our willingness to permit a market: The social costs of indentured labor, for example, surely include one's outrage at inducing the poor to sell themselves, and this cost must be considered before the society allows peonage. The willingness of a poor man, confronting a tragic situation, to choose money rather than the tragically scarce resource always represents an oblique indictment of society's distribution of wealth. That willingness, when it follows a first-order determination which has been made collectively, is a yet more insistent accusation; it presents the wrenching spectacle of a rich man and a poor man bidding against each other for it. Yet the degree of redistribution of wealth necessary to avoid such external costs would itself be too costly. It might require a virtual equivalence of wealth such that incentives to produce would not survive.

The tragedy of the choice is the basis for adoption of a conservative attitude that urges society to avoid the risks of introducing untried technologies. The conservative attitude has both a substantive and a procedural dimension. Substantively, it asserts categorically that it is wrong to subject persons to certain risks. Procedurally, it places the burden of proof on advocates of technological innovation and requires that change be held in abeyance pending the production of information necessary to a rational assessment of the innovation's net value to society.

Distinctions among the protechnical, analytical, and conservative attitudes as discussed above are essential to understanding the role of the legal system in setting rules for pesticide regulation. But it must be realized that the political process is too dynamic and flexible to fix consistently on one attitude to the exclusion of others. Because the stakes are high in pesticide regulation, the decision-making process can accommodate diverse interests only through compromise. For this reason, laws regulating the entry of pesticides into the market and their subsequent use reflect simultaneously all three of the above attitudes. The task of implementing the compromise legislation is then delegated to an administrative agency—EPA. The legislation tells the Agency that pesticides are to be assessed rationally, that some risk is acceptable, but that in any given case the Agency may be conservative in deciding to prefer risk avoidance over economic benefits: in short, that EPA has great but not unlimited discretion to regulate pesticides.

Knowledge of the background and structure of the laws regulating pesticides is essential to understanding the problem with which this report is concerned: How can EPA improve its procedures for rational evaluation and regulation of pesticides? The problem is at one level a technical one; at another level it is a question of consensus about issues. But the consensus does not exist.

EARLY LEGISLATION: CONSUMER PROTECTION

Pesticide regulation developed in an atmosphere that presumed that the application of technology was beneficial. Subsequent legislation has challenged, but not supplanted, the earlier legislation based on this assumption, although the first two statutes regulating pesticide manufacture and use were classic examples of consumer protection legislation.

Chemical pesticides came into widespread use toward the end of the nineteenth century. The formulas were simple and the compounds were sold by many small, often itinerant dealers, or mixed by farmers themselves with products ordered by mail. The fragmented market made it easy to pass off adulterated goods, and this state of affairs alarmed Congress in 1910. In response to pressure from the U.S. Department of Agriculture (USDA) and farm organizations, a simple statute was passed in 1910 specifying the percentage of certain ingredients for Paris green and lead arsenate (arsenical pesticides) and setting general standards for other insecticides or fungicides. Enforcement was *ad hoc*, as the evidence necessary to prove a violation of the statute was collected only by random plant inspections or through user complaints. The Insecticide Act of 1910, therefore, had a limited purpose—the protection of consumers from fraudulent goods—but the purpose was seen as an adequate response to the problem until 1947.

Pesticide compounds ceased to be simple by the end of World War II as synthetic organic pesticides came into widespread domestic use. The new chemicals were more toxic, and valuable nontarget species were vulnerable to damage if the pesticide was not used with care. Congress, therefore, felt that there was a need to provide users with the advance information necessary to make informed choices. The Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (FIFRA) required for the first time that all pesticides be registered before they could be marketed and that the label specify the content. This law is an extension of classic consumer protection objectives. A rational user is assumed and the problem is defined as the disclosure of sufficient information for the user to make an informed choice.

The crucial assumption underlying FIFRA was that the major problem associated with the use of pesticides was their efficacy. The major basis for denying registration was that the label contained claims that differed from those made to the USDA. The only protection against undesirable effects of the pesticide on nontarget species and plants was afforded by the requirement that the label identify the pesticide as a poison. The USDA administered FIFRA on the assumption that efficacy was the major problem and, as a consequence, the bulk of the USDA's regulatory activity was concerned with ensuring that pesticides were labeled accurately. Few chemicals were barred from the market.

SHIFT TO HEALTH AND ENVIRONMENTAL PROTECTION

The assumption that efficacy was the principal problem was challenged in the 1960s, first by Rachel Carson's *Silent Spring* (1962) and then by a series of presidential commissions. These challenges led to the current laws.

The basic argument raised by critics of pesticide use is that the major problem is safety, not efficacy: pesticides are potentially unsafe because they have unanticipated effects on nontarget species, and thereby pose risks to ecosystem stability and to human health. The problem can be solved only partially by the disclosure of impact information. A full solution requires that some pesticides be barred from the market or have limits placed on the circumstances in which they can be used. Theoretically, this solution was possible under FIFRA because the statute had established three review points for a pesticide: (1) registration, where the chemical was screened prior to market entry; (2) suspension, a quasi-summary removal from the market; and (3) cancellation of a registration, which resulted in permanent removal from the market. However, as administered by the USDA, there was no substantial safety review at any of these three stages. In part, the lack of adequate safety review was caused by 1947 legislation that allowed a registrant whose chemical was challenged to obtain a protest registration, thereby shifting the burden of proving a pesticide ineffective or unsafe to the government and allowing the challenged chemical on the market.

In the 1960s, a two-pronged attack was made against USDA's interpretation of FIFRA and on the adequacy of the legislation itself. FIFRA was attacked by both the courts and Congress. Each branch of government produced a reform of pesticide law, but the reforms were not identical. The divergence between the approaches of the Congress and the courts accounts for the tension in EPA's current regulatory policy and the continuing controversy that surrounds the scope of pesticide regulation.

The courts adopted a conservative strategy by giving the USDA and, subsequently, EPA the discretion to ban pesticides on the basis of a comparison of benefits and risks that took a very conservative view of socially acceptable risk. Congress accepted the necessity of basing decisions upon risk as opposed to proof of harm, but attempted to ensure that risk would be only one of the relevant factors considered by EPA. To this end, Congress imposed a process that based all decisions on a balanced benefit-cost analysis derived from neoclassical welfare economics. These two strains of reform—the courts' and Congress's—form the basis of EPA's current regulatory policy. An appreciation of the related but distinct nature of each is essential to understanding the problems that EPA is now facing in subjecting pesticides to a rational benefit-risk analysis.

The Role of Congress

Congress reformed FIFRA in two stages. In 1964, protest registrations were eliminated and the definition of a misbranded pesticide was expanded to include pesticides that would injure invertebrate animals, as well as vertebrates and plants valuable to man. The 1964 amendments expressly directed the USDA's attention to safety considerations for the first time. Eight years later, FIFRA was supplemented by the Federal Environmental Pesticide Control Act of 1972 (FEPCA).

FEPCA did not eliminate the consumer protection objectives of the earlier statute, but supplemented them with the recognition that the public generally needed to be protected from potentially harmful effects of pesticide use. The heart of EPA's expanded mandate is Section 3(c)(5), which requires the Agency to refuse to register a pesticide unless it is determined that "when used in accordance with widespread and commonly accepted practice it will not cause unreasonable adverse to the Secretary of Agriculture at least 60 days before they are issued, and if the Secretary comments in writing within 30 days, the comments must be published in the *Federal Register*.

The Scientific Advisory Panel was created to review health and environmental hazard assessments with the intent to provide unbiased and objective opinion on the risk side. The thought was to put a check on EPA's use of a line of reasoning that held that lack of knowledge about effects is a valid basis for banning a chemical in order to err on the side of safety. Proposed cancellation and suspension notices are sent to the Scientific Advisory Panel, and the Panel's comments are published along with those of the Secretary of Agriculture. Upon a finding of imminent hazard to human health, however, the Administrator may waive the notice and comment procedure for a suspension proceeding.

The conclusion that emerges from the legislative history is that Congress recognized that a certain level of risk is inevitable in pesticide use and that the presence of risk is not sufficient reason to deny or cancel the registration of a pesticide.

The Role of the Courts

At the same time, however, the courts were developing the doctrine that risk alone is sufficient grounds for denying or cancelling a registration. The doctrine evolved in a series of decisions reviewing USDA and, subsequently, EPA decisions to suspend and cancel registrations. What these decisions did was to set a conservative risk standard to determine what evidence would *trigger* a benefit-risk analysis and, then, to hold that the *trigger* evidence would be a sufficient basis to support a *final* conclusion that the risks exceeded the benefits. Only secondary attention was required for benefits. This is the assumption behind the Rebuttable Presumption Against Registration (RPAR) process (described later in this chapter). RPAR rules stem much more from the pesticide precedents in the U.S. Court of Appeals for the District of Columbia Circuit than from Congress, as the 1978 amendments to FEPCA illustrate.

The first issue the courts were required to decide was when the USDA had a duty to suspend a chemical and institute cancellation proceedings under FIFRA. The issue arose in 1969, when the Environmental Defense Fund (EDF) petitioned the USDA to cancel all DDT registrations and the USDA refused. The 1964 legislation required the USDA to suspend a pesticide and institute cancellation proceedings if suspension were necessary to "prevent imminent hazard." In a major decision interpreting the phrase, the court transformed FIFRA from a consumer protection to a regulatory statute by holding that once a substantial question of safety was raised, the burden of proof shifted to the manufacturer to justify continued registration (EDF v. *Ruckelshaus* 1971). This burden has been described as "heavy" (EDF v. *U.S.* EPA 1971) in that it requires the registrant to establish the safety of a pesticide. Similarly, another court said that "once risk is shown, the responsibility to demonstrate that the benefits (of continued use) outweigh the risks is a heavy one . . . " (EDF v. *U.S.* EPA 1976).

A risk analysis often hinges on important but abstruse debates among scientists about the permissible inferences that can be drawn from laboratory experiments. In such situations, the most the courts can do is attempt to understand the issues, make sure that the Agency has considered all relevant factors and that all parties have had adequate and real participation in the decision process, insist that the Agency has disclosed the basis of its reasoning sufficiently to permit a court to conclude that the decision *follows* from the evidence, and make sure that there is some objective basis for the decision. However, in the end, as long as EPA bases its cancellation or suspension decisions on a risk analysis that has respectable scientific support, its discretion is practically unreviewable. In the heptachlor-chlordane suspension decision, the U.S. Court of Appeals for the District of Columbia Circuit announced the following standard:

> An ultimate finding in a suspension proceeding that continued use of challenged pesticides poses a "substantial likelihood of serious harm" must be supported by substantial, but not conclusive, evidence. In evaluating laboratory animal studies on heptachlor and chlordane there was sufficient "respectable scientific authority" upon which the Administration could rely in determining that heptachlor and chlordane were carcinogenic in laboratory animals.
>
> Human epidemiology studies so far attempted on chlordane and heptachlor gave no basis for concluding that the two pesticides are safe with respect to the issue of cancer. To conclude that they pose a carcinogenic risk to humans on the basis of such a finding of risk to laboratory animals, the Administrator must show a causal connection between the uses of the pesticides challenged and resultant exposure of humans to those pesticides. He made that link by showing that widespread residues of heptachlor and chlordane are present in the human diet and in human tissues. Their widespread occurrence in the environment and accumulation in the food chain is explained by their chemical properties of persistence, mobility and high solubility in lipids (the fats contained in all organic substances). Residues of chlordane and heptachlor remain in soils and in air and aquatic ecosystems for long periods of time. They are readily transported by means of vaporization, aerial drift, and run-off of eroding soil particles. The residues have been consistently found in meat, fish, poultry and dairy products monitored in the FDA Market Basket Survey and are also frequent in components of animal feeds. This evidence supports a finding that a major route of human exposure is ingestion of contaminated food-stuffs. EPA's National Human

> Monitoring Survey data show that heptachlor epoxide and oxychlordane, the principal metabolites of heptachlor and chlordane respectively, are present in the adipose tissue of over 90% of the U.S. population. (EDF v. *U.S.* EPA 1976)

The other side of a benefit-risk analysis is an evaluation of the benefits of a pesticide's use. Welfare economics has made some progress in developing benefit-cost (or risk) procedures that can be applied to pesticide decisions. EPA has generally argued that its mission is to protect the public from environmental harm, and thus it is entitled to devote more attention to the risks of an activity than to its economic benefits. EPA's general policy has never been directly challenged in the courts, but there are indications that the courts may define with some precision the duty to consider benefits as the choices the EPA must make become harder.

When the court reviewed the aldrin-dieldrin suspension hearing, it was the first time that the court considered EPA's duty to assess benefits, and out of this case a rather casual attitude toward benefits developed: a suspension was analogized to a preliminary injunction (a decision before a court decides the merits). The duty to consider a suspension arises when any substantial question about a pesticide's safety is posed. When this occurs, EPA is obliged to suspend whenever there are no offsetting benefits to the public. Therefore, the Administrator has not exercised his or her discretion properly unless he or she has given adequate consideration to benefits. The court's standard makes it clear, however, that the court is interested primarily in a discussion of benefits that is basically adequate to support a suspension decision, but it does not expect a rigorous analysis:

> The Administrator's mere mention of these products' major uses, emphasized by the EPA, cannot suffice as a discussion of benefits, even though "the data before him . . . reflected the view that aldrin-dieldrin pesticides are the only control presently available for some twenty insects which attack corn and for one pest which poses a real danger to citrus orchards. . . . " (Brief for EPA:19)
>
> The interests at stake here are too important to permit the decision to be sustained on the basis of speculative inference as to what the Administrator's findings and conclusions might have been regarding benefits. Sound principle sustains the practice of vesting choice of policy with the Administrator. Its corollary is that the specific decision must be explained, not merely explainable, in terms of the ingredients announced by the Administrator as compromising the Agency's policies and standards. This is the case even though the variables of the policy approach selected by the Administrator are not necessarily required by the underlying statute.
>
> Our conclusion that a mere recitation of a pesticide's uses does not suffice as an analysis of benefits is fortified where, as here, there was a submission, by EDF, that alternative pest control mechanisms are available for such use. The analysis

> of benefit requires some consideration of whether such proposed alternatives are available or feasible, or whether such availability is in doubt. (EDF v. *U.S.* EPA 1972)

In subsequent cancellation and suspension cases, the adequacy of benefit analyses has been given secondary emphasis, although the duty to consider benefits is higher in the former than in the latter. This secondary emphasis is given because (1) the benefit claims have often been raised by manufacturers without adequate evidence, and (2) alternative chemicals have been available. For example, in the heptachlor-chlordane suspension hearing, the Administrator's benefit analysis of use on corn was sustained on this ground:

> Heptachlor and chlordane were used on an estimated 3.5% of the total corn acreage in the United States in 1975, largely in an effort to control black cutworm. Cutworms sporadically infest 2 to 8% of total U.S. corn farms, and occur most often in lowland, river bottom areas. Chlordane and heptachlor are used as preplant treatments to insure against possible infestations. The Administrator found, with record support, that no macro-economic impact will occur as a result of suspending those pesticides. He also found that crop surveillance or "scouting" for infestations during the early weeks of plant growth, together with application of post-emergence baits or sprays where necessary, provide an effective alternative to the more indiscriminate prophylactic use of chlordane and heptachlor. Velsicol urges that this approach is not as effective as the persistent protection provided by chlordane. Especially in the absence of proof of a serious threat to the nation's corn, there is no requirement that a pesticide can be suspended only if alternatives to its use are absolutely equivalent in effectiveness. The Administrator reasonably took into account that a transition period would be necessary to implement post-emergent techniques of control and concluded that the challenged pesticides could continue in use for corn protection until August 1, 1976. This evaluation of alternatives and the time required to implement them is supported by substantial evidence, and we find no basis to disturb the Administrator's balancing of costs and benefits. (EDF v. *U.S.* EPA 1976)

However, the attitude of giving secondary attention to benefits is changing for institutional and legal reasons. As pesticide issues become more difficult to resolve, and better benefit evidence is generated, the hard-look doctrine, which courts follow with respect to judicial review, may require EPA to present a more technically acceptable benefit component of the benefit-risk analysis. A benefit advisory panel to parallel the Scientific Advisory Panel might do much to strengthen EPA's benefits presentation (see Chapter 5).

A recent circuit court decision on an issue not involving pesticides illustrates the possible procedural impact of such a panel. *Seacoast Anti-*

Pollution League v. *Costle* (1978) held that the Administrator cannot use a technical panel's recommendation as the basis for his or her decision when the technical panel's assertions rest on scientific literature not introduced into evidence in the hearing. Seacoast held, in effect, that if an expert advisory panel is asked for a recommendation, the conclusions on which the recommendation is based must be documented with evidence consistent with the state of the art. Seacoast further suggested that the use of advisory panels will require the Administrator to weigh a panel recommendation carefully or run the risk that a decision will be remanded for failure to justify departures from the recommendations. Formally, of course, science advisory panels cannot bind the Administrator, since the issues at stake in a pesticide regulatory decision are ones of policy. However, in subtle but significant ways, a technical panel shapes the issues and the weighing of the evidence.

To summarize, from 1910 to the present, federal pesticide legislation has evolved from largely a registration to primarily a regulatory statute affording greater protection to both human health and the environment. The legislation of 1910 and 1947 was basically concerned with consumer protection. In the 1960s and early 1970s, the need was recognized to evaluate a pesticide's safety and to remove unsafe pesticides from the market. The 1972 legislation provided the framework for weighing the benefits of using a pesticide (theretofore unquestioned) against the risks it entails, and for cancelling unsafe pesticide uses. It required that all the pesticides then registered, some 35,000, be reviewed under the newly established standards of safety. In the mid-1970s judicial decisions seemed to weigh risks more heavily than benefits. As a result, in 1975 and 1978 additional legislation was enacted in an attempt to restore the balance between risk and benefit considerations. Recent court decisions appear to be moving in that direction.

THE RPAR PROCESS: A DESCRIPTION

The preceding discussion of the legislative framework describes the evolution of EPA's current mandate to protect public health and the environment from "unreasonable adverse effects" of pesticide use. The mandate is interpreted to authorize an evaluation and weighing of costs (or risks) and benefits to be used in determining whether a pesticide should be registered, reregistered, or cancelled. The following discussion describes EPA's current procedures (as of mid-1979) for implementing that mandate, namely, the Rebuttable Presumption Against Registration (RPAR) process. The RPAR process was adopted in late 1975, and it is a key part of EPA's plan to review the approximately 35,000 pesticide formulations on the U.S. market, as well as any new registration applications. It should be recognized, however, that despite the time elapsed, the full process is only in the incipient stage, in that it has been initiated less than thirty times and completed only seven.

THE CONCEPT

Regulations for the registration, reregistration, and classification of pesticides under FIFRA, as amended in 1972, were developed by EPA and are set forth in the *Code of Federal Regulations* (CFR), Title 40, Part 162. The regulations establish a mechanism for identifying and evaluating those pesticides that appear to cause unreasonable adverse effects on human health and the environment. The initial step in this determination considers risk only. Each pesticide, and its metabolites or degradation products, is measured against a set of risk criteria, or *triggers*, set forth in 40 CFR 162.11.[1] Paraphrased, these criteria are:

1. *Acute toxicity* in humans, domestic animals, or nontarget wildlife (measured by formulas for lethal doses);
2. *Chronic toxicity* determined by oncogenic effects induced in humans or in experimental animals as a result of oral or dermal exposure, or inhalation; mutagenic effects induced, as determined by multitest evidence; any other chronic effects produced in test animals; anticipated significant population reduction in nontarget organisms; or anticipated fatality to endangered species; or
3. *Absence of an antidote or other emergency treatment* for toxic effects in humans from a single exposure to the pesticide.

If a pesticide reaches or exceeds these risk criteria, EPA's Office of Pesticide Programs (OPP) is obligated to issue an RPAR and weigh benefits against risks. An RPAR can be issued only if one or more of the risk criteria are reached or exceeded.

The RPAR process provides a structure for intensive scientific review and public comment on the risks and benefits of any questionable compound before a decision is made on whether to allow its continued use. It is important to understand that the RPAR process is an operational tool; it is used for applying an evaluative methodology—benefit-risk analysis. (See Chapters 4, 5, and 6 for a discussion of methodologies for explicitly evaluating and comparing risks and benefits.) The RPAR approach attacks the problem of evaluating pesticide registration and reregistration applications on a one-by-one (compound-by-compound) basis. Once OPP determines that a specific pesticide formulation exceeds the risk criteria described above, the compound enters the RPAR process and becomes the focus of an extensive "wall-to-wall" review in which properties, effects, benefits, and risks are evaluated for each use of the compound (J. Carley, EPA Office of Pesticide Programs. Presented at Association of American Pesticide Control Officials meeting, April 4, 1978, Washington D.C.).

The number of compounds that can undergo such extensive analysis is necessarily small because of EPA's limited resources, and the RPAR process has subsequently turned into a bottleneck in registration and reregistration procedures. In an attempt to relieve the bottleneck, EPA is planning by mid-1981 to merge the RPAR process into a generic standards program, authorized in the Federal Pesticide Act of 1978. Under the latter program the focus of the risk and benefit evaluation will be shifted from one specific formulation to the active ingredient and all the pesticide formulations in which it occurs (U.S. EPA 1978). Data on its toxicology, chemistry, effects on fish and wildlife, residues, movement, and fate will be examined for each active ingredient, and a monograph will be prepared for use in developing generic standards for all formulations using the ingredient. The same basic ingredients appear repeatedly, singly or in combination, in the 35,000 pesticide formulations for which reregistration is being sought. Edwin Johnson, head of EPA's pesticide program, told a meeting of the Association of American Pesticide Control Officials in Williamsburg, Virginia, August 10, 1978, that most large-volume, food-use pesticides can be regulated by about 200 generic standards; all active registrations can be handled by 514 standards; and only about 65 active ingredients are of major significance (on the basis of volume of production, number of registered products in which they appear, tolerances issued, and volume and type of use). Development of generic standards began in late 1978, with 47 scheduled for completion, and another 50 scheduled for initiation, in 1980 (Pesticide & Toxic Chemical News 1979).

It is important to realize that the generic standard process will not change the current concepts of decision making in OPP but is intended to eliminate the need for repetitive review of complex toxicological, metabolic, and environmental transport and fate data for each pesticide formulation. The methodology for evaluating risks and benefits and weighing them against each other will be the same, though the plan is to change the structure for applying the methodology.

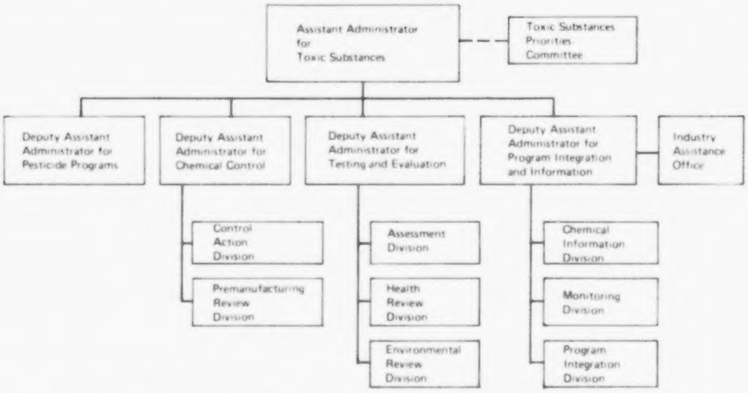

Assistant Administrator for Toxic Substances
Toxic Substances Priorities Committee
Deputy Assistant Administrator for Pesticide Programs
Deputy Assistant Administrator for Chemical Control
Deputy Assistant Administrator for Testing and Evaluation
Deputy Assistant Administrator for Program Integration and Information
Industry Assistance Office
Control Action Division
Premanufacturing Review Division
Assessment Division
Health Review Division
Environmental Review Division
Chemical Information Division
Monitoring Division
Program Integration Division

FIGURE 2.1 Organization of EPA Office of Toxic Substances, April 1978.

ADMINISTRATIVE RESPONSIBILITY

Primary responsibility for regulating pesticides lies with OPP, one of four major units in the Office of Toxic Substances (see Figure 2.1). The line of administrative responsibility for regulating pesticides currently runs from the Deputy Assistant Administrator of OPP, to the Assistant Administrator of the Office of Toxic Substances, to the EPA Deputy Administrator and the Administrator. Other branches of EPA that assist OPP are the Office of General Counsel, the Office of Enforcement, the Office of Research and Development, and the Carcinogen Assessment Group (CAG).

OPP has 11 functional units (see Figure 2.2). The roles played in the RPAR process by most of these units are discussed later in this chapter. The RPAR process is administered by the Special Pesticide Review Division (SPRD) within OPP and is set in motion when the director of SPRD accepts a pesticide as a candidate for an RPAR. The current mechanism for identifying RPAR candidate compounds and selecting the order of RPAR's is discussed in Chapter 3.

When a compound becomes an RPAR candidate, it is assigned to a project manager within SPRD. Each project manager has the responsibility for managing a specific RPAR case from beginning to end, i.e., from the determination that an RPAR appears to exist, through the Administrator's final determination and hearings (if any). The project manager assembles a project support team (hereafter referred to as the RPAR team) using scientific personnel from all of OPP, with an attorney assigned to represent the Office of General Counsel. This is the group that, using

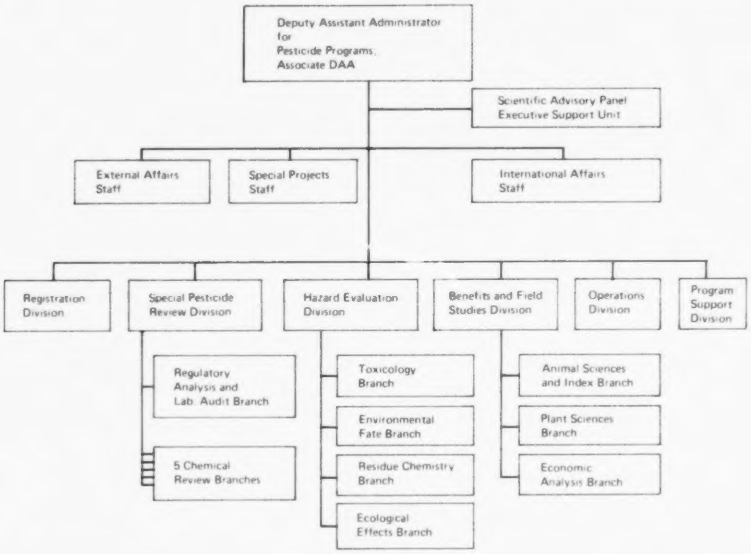

Deputy Assistant Administrator for Pesticide Programs; Associate DAA
Scientific Advisory Panel Executive Support Unit
External Affairs Staff
Special Projects Staff
International Affairs Staff
Registration Division
Special Pesticide Review Division
Hazard Evaluation Division
Benefits and Field Studies Division
Operations Division
Program Support Division
Regulatory Analysis and Lab. Audit Branch
5 Chemical Review Branches
Toxicology Branch
Environmental Fate Branch
Residue Chemistry Branch
Ecological Effects Branch
Animal Sciences and Index Branch
Plant Sciences Branch
Economic Analysis Branch

FIGURE 2.2 Organization of EPA Office of Pesticide Programs, April 1978.

such external resources as the CAG, the USDA, and contractors, actually conducts the RPAR analyses. A representative from the Office of General Counsel takes an active role in the development of pesticide documents, regulatory options, and official RPAR notices.

The project manager also chairs a working group that is assembled for a specific RPAR compound. This group is distinct from the RPAR team and is composed of representatives from other EPA offices, for example, the Offices of Research and Development, Enforcement, General Counsel, Planning and Management, and frequently CAG. The working group is responsible for preparing RPAR notifications and *Federal Register* notices, identifying needed scientific reviews, and working with internal and external scientific review groups. In principle, this working group is to provide the first level of agency-wide administrative and policy review of the benefit-risk assessment and to ensure internal agency coordination. However, it appears that the working group rarely meets as an entity, and the degree to which it plays a role in the RPAR process is unclear. The project manager often discharges most of the working group's responsibilities.

A second level of internal agency review is provided by the Pesticide Chemical Review Committee (PCRC). PCRC is a standing committee composed of the same type of representatives as the working groups; often PCRC and working group members overlap. As is the case with the working group, it is unclear to what extent PCRC plays a role in the RPAR process; the extent may vary with the specific RPAR.

THE SCHEDULE: PUBLIC DEADLINES AND POSITION DOCUMENTS

The Agency's position with respect to a compound as it moves through the RPAR process is set forth in a series of Position Documents (PD's); their general focus is as follows: PD 1—preliminary risk assessment, PD 2—response to rebuttals, PD 3—benefit-risk analysis, and PD 4—final Agency decision. Position Documents 1 and 4 are published in the *Federal Register* in support of and together with the official notification of a rebuttable presumption against registration and continued registration and the final notice of determination, respectively. The proposed determination concluding the RPAR is also published in the *Federal Register* prior to the final notice. Position Documents 2 and 3, in support of the proposed determination, are publicly available (and are frequently combined into one document, PD 2/3), but are not usually published in the *Federal Register*.

Figure 2.3 shows the major milestones in the ideal RPAR schedule. It should be noted that the ideal has not yet been met in practice. The RPAR activities begin well in advance of PD 1. The collection of data to support PD 1 (use and hazard information) begins as soon as an RPAR candidate has been ranked against the other candidates and has found its place in the RPAR queue. Review of the compound is not scheduled until the initial data package is complete. The data collection, review, and validation is generally a long process, usually involving many months. Ninety days after the data package is complete, a decision is due on whether to issue an RPAR on the chemical.

Only if a pesticide meets or exceeds one or more of the risk criteria mentioned earlier is an RPAR issued. An RPAR notification is sent by registered letter to affected registrants, stating that the compound is being presumed against and why. The notice is also published in the *Federal Register* together with PD 1, and a copy of the published notice is sent to the USDA, other federal agencies, user groups, industry associations, and environmental groups. PD 1 presents the data supporting issuance of the RPAR.

Issuance of the RPAR starts a time clock for all subsequent steps. Registrants and other interested parties are given 45 days to offer rebuttal evidence; a registrant may seek to extend this period by 60 days by showing good cause. An RPAR may be rebutted by showing that (1)

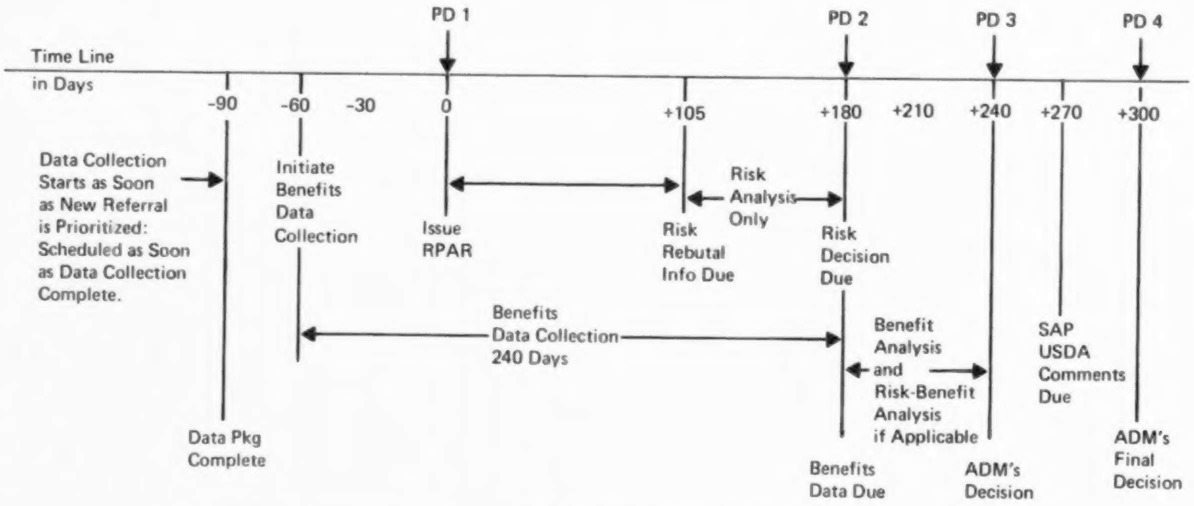

PD 1
PD 2
PD 3
PD 4
Time Line
in Days
-90
-60
-30
0
+105
+180
+210
+240
+270
+300
Data Collection Starts as Soon as New Referral is Prioritized: Scheduled as Soon as Data Collection Complete.
Initiate Benefits Data Collection
Issue RPAR
Risk Rebutal Info Due
Risk Analysis Only
Risk Decision Due
Benefits Data Collection 240 Days
Benefit Analysis and Risk-Benefit Analysis if Applicable
SAP USDA Comments Due
Data Pkg Complete
Benefits Data Due
ADM's Decision
ADM's Final Decision

FIGURE 2.3 RPAR major milestone schedule, 1977. Source: Modified from U.S. EPA (1977a).

EPA erred in determining that the pesticide meets or exceeds the risk criteria in 40 CFR 162.11; (2) any risk that exists can be reduced to such an extent that significant adverse effects are unlikely to occur; or (3) benefits of using the pesticide exceed the anticipated risks. By the time 180 days have elapsed, EPA is supposed to have determined whether all risks have been rebutted. A second Agency position document may be issued at this point presenting EPA's analysis of the rebuttals. If the risks are rebutted, the RPAR is cancelled, and PD 2 is issued. More commonly, however, if all risks have not been rebutted, PD 2 and PD 3 are issued jointly in one document. PD 3 is issued together with a notice of the proposed determination concluding the RPAR ("notice of intent") and presenting the benefit-risk analysis supporting the proposed action.

The collection of benefit data, like risk data, begins well before PD 1 is issued, even though the benefit assessment does not appear in a position document until PD 3. The benefit assessment procedure is a joint effort between USDA and EPA. Current USDA/EPA procedures provide for the establishment of a joint assessment team as soon as OPP announces an intention to issue an RPAR. In practice, the procedure will usually allow teams to be formed approximately 60–90 days prior to issuance of the RPAR. The collection of benefit data is supposed to be completed within 180 days of issuance of the RPAR. An additional 60 days is then provided for completion of the analysis, although extension of this deadline is frequently necessary. The proposed determination and PD 3 (or PD 2/3) are issued upon completion of the independent risk and benefit assessments, supposedly 240 days after the initial RPAR notice.

Sixty days before the Agency plans to issue a final determination, the proposed action and supporting position document (PD 3 or 2/3) are sent to the independent FIFRA Scientific Advisory Panel (SAP) and the USDA for their review as required by the 1975 amendments to FIFRA. (The scientific review given to the risk and benefit assessments is described later in this chapter.) If comments are received within 30 days, the comments and EPA's response are published in the *Federal Register* with the proposed regulation. Thirty days after comments are received, EPA's Administrator is supposed to issue the final determination, supported by PD 4.

Of the above deadlines, only the rebuttal period and the final external (USDA and SAP) review period are Congressionally imposed, and even there, some flexibility is allowed. In 1977, EPA estimated 4 1/2 months (135 days) between rebuttals and PD 2/3, making the total time from PD 1 to PD 4 roughly 300 days (see Figure 2.3). In fact, however, delays occur at each step of the process, extending the deadline indefinitely.

THE ANALYSIS

The preceding sections have described the framework into which the actual activity flows involved in conducting the risk and benefit evaluations fit. In practice, the purpose of the RPAR process is to provide a decision maker with information on the trade-offs between risks and benefits associated with regulatory options for each RPAR pesticide. This section describes the sequence of steps and the organizational arrangements involved in the development of an RPAR decision document. Details of the methods used in the various analyses that ultimately constitute the risk and benefit assessments are described in Chapters 4 and 5, respectively.

The major participants in an RPAR analysis are the project manager and the RPAR team. The project manager coordinates and synthesizes the benefit and risk assessment activities carried on by the members of the RPAR team. In accordance with the Administrator's *Health Risk and Economic Impact Assessments of Suspected Carcinogens: Interim Procedures and Guidelines* (U.S. EPA 1976), benefit and risk assessments are conducted separately. Thus, when the management, risk, and benefit components are considered together, a tripartite flow of activities results. The basic steps involved in these activity flows are presented in Figure 2.4 (see Figure 2.3 for the related time schedule). It should be emphasized that there is continuous communication and interaction among individuals from each activity stream.

Organizational Arrangements

Risk Assessment Lead organizational responsibility for conducting risk assessments in OPP lies with the Hazard Evaluation Division (HED), which is divided into four branches: Toxicology, Environmental Fate, Residue Chemistry, and Ecological Effects. Table 2.1 shows the major components of OPP's risk assessment and the lead organizational responsibilities. The HED is responsible for analyzing human exposure and human health and ecological hazards associated with pesticide use. Throughout the RPAR process, technical competence is provided both by HED staff and outside consultants.

While HED is responsible for assessing acute and chronic hazards, investigation and analysis of cancer hazard is delegated to CAG, an agency-wide group that focuses on predicted human risks from exposure to suspected carcinogens. Cancer risk assessments made by CAG are submitted to HED for further review and evaluation. In cases where carcinogenicity is the only hazard, HED provides the exposure analysis and retains review and evaluation responsibilities for the risk assessments prepared by CAG. There is, however, a move within the Agency to centralize risk assessment, and changes in the organizational arrangements described above can be expected.

A close, informal working relationship is maintained between HED and OPP's Benefit and Field Studies Division (BFSD). The primary aim of this interaction is to enhance HED's understanding of basic pesticide formulation and to use concepts as they relate to areas of potential risk. The interaction also provides insight into the feasibility of various regulatory options being considered by HED. Such insight is important when the issue of enforceability of proposed regulatory options is taken into account.

Benefit Assessment Lead organizational responsibility for conducting benefit analysis in OPP lies with BFSD, which is divided into three branches that are organized along disciplinary lines: Animal Science and Index, Plant Sciences, and Economic Analysis. Table 2.2 shows the major components of OPP's pesticide benefit analysis and the lead organizational responsibilities for analysis. The general guidelines for the joint EPA and USDA benefit assessment effort are presented in a 1976 "Memorandum of Understanding between the U.S. Department of Agriculture and the U.S. Environmental Protection Agency" and an October 1977 supplement to that memorandum.

A key element of the guidelines is a provision for establishing a joint assessment team for gathering and analyzing benefits data. The assessment teams (officially referred to as the USDA/State/EPA Benefit Assessment Teams and hereafter abbreviated to USDA/EPA) consist of representatives from USDA, state departments of agriculture and agricultural colleges (extension service and experimental station personnel), and EPA. The USDA, state, and college representatives—including the team leader—are selected by the USDA (through the Pesticide Coordinator, Office of Environmental Quality Activities, USDA). The EPA personnel are appointed by the BFSD within OPP. The size of the team varies from about three to fifteen, depending upon the complexity of the assessment.

An important function of the state and agricultural college people, who are usually biologists, is to develop the basic biological information (e.g., yield effects) and, to some extent, the economic data (e.g., price per pound of active ingredient) necessary for conducting a benefit analysis. In addition, the extension and experimental station experts frequently provide information (e.g., method of application) useful in exposure analyses. These data are gathered through a combination of literature searches and personal communications with various agricultural experts

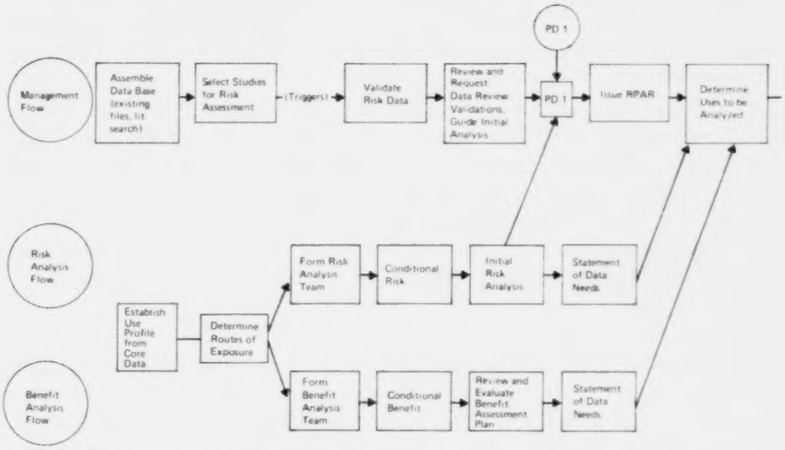
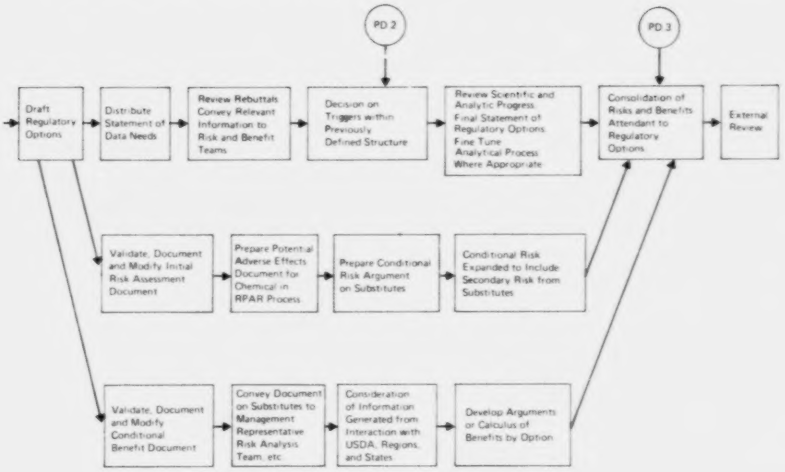

Management Flow
Assemble Data Base (existing files, lit. search)
Select Studies for Risk Assessment
(Triggers)
Validate Risk Data
Review and Request Data Review Validations, Guide Initial Analysis
PD 1
PD 1
Issue RPAR
Determine Uses to be Analyzed
Risk Analysis Flow
Benefit Analysis Flow
Establish Use Profile from Core Data
Determine Routes of Exposure
Form Risk Analysis Team
Conditional Risk
Initial Risk Analysis
Statement of Data Needs
Form Benefit Analysis Team
Conditional Benefit
Review and Evaluate Benefit Assessment Plan
Statement of Data Needs

FIGURE 2.4 **Tripartite activity flow (sequence of steps) in support of the RPAR process. Source: Keaney (1977).**

TABLE 2.1 Components of Pesticide Risk Assessment and Principal Organizational Responsibilities in the Office of Pesticide Programs

Component	HED Branch
Background	
Chemical and physical properties	Residue Chemistry
Environmental fate and persistence	Environmental Fate
Human exposure analysis	
Dermal	Environmental Fate
Respiratory	Environmental Fate
Dietary (food and water)	Residue Chemistry
Inhalation, penetration and absorption rates	Toxicology
Human health risk	
Cancer	CAG,[a] Toxicology
Acute toxicity	Toxicology
Other chronic toxicity	Toxicology
Ecological hazard	Ecological Effects

[a] Not a branch of HED.


PD 2
PD 3
Draft Regulatory Options
Distribute Statement of Data Needs
Review Rebuttals Convey Relevant Information to Risk and Benefit Teams
Decision on Triggers within Previously Defined Structure
Review Scientific and Analytic Progress Final Statement of Regulatory Options Fine Tune Analytical Process Where Appropriate
Consolidation of Risks and Benefits Attendant to Regulatory Options
External Review
Validate, Document and Modify Initial Risk Assessment Document
Prepare Potential Adverse Effects Document for Chemical in RPAR Process
Prepare Conditional Risk Argument on Substitutes
Conditional Risk Expanded to Include Secondary Risk from Substitutes
Validate, Document and Modify Conditional Benefit Document
Convey Document on Substitutes to Management Representative Risk Analysis Team, etc
Consideration of Information Generated from Interaction with USDA, Regions, and States
Develop Arguments or Calculus of Benefits by Option

(reviewed in Chapter 5). Finally, it appears commonplace for some of the agricultural college (or perhaps USDA) people to have a background in toxicology or allied fields, thereby allowing the joint assessment team to comment on EPA's risk assessment. The economic impact assessment is usually a joint effort by economists from both USDA (Economics, Statistics, and Cooperatives Service) and EPA (Economic Analysis Branch, BFSD, OPP).

Before the official report of the assessment team is forwarded to OPP, it must be approved by a variety of USDA officials, including the Secretary of Agriculture. However, the terms of the Memorandum of Understanding allow each agency to reach independent assessments if necessary; consequently, OPP is not bound to rely only upon the findings of the USDA/EPA assessment teams. The joint assessment team can be reactivated by USDA if further data collection or analysis becomes necessary.

Benefit-Risk Analysis The SPRD, in the person of the project manager, has responsibility for coordinating the risk and benefit analyses and for assembling appropriate decision-making (position) documents based on contributions from various offices in OPP. SPRD is composed of five chemical review branches and a Regulatory Analysis and Laboratory Audit Branch. At the conclusion of the benefit and risk assessments, an effort to weigh the benefits and risks is undertaken by the RPAR team under the general supervision of SPRD's Regulatory Analysis Branch. The

TABLE 2.2 Components of Pesticide Benefit Analysis (for a given site) and Principal Organizational Responsibilities in the Office of Pesticide Programs

	BFSD Branch	
Component	Insecticides/ Rodenticides	Herbicides/ Fungicides
Current use analysis		
EPA registrations of RPARs and alternatives	ASIB[a]	PSB[b]
Recommendations for use of RPAR and alternatives	ASIB	PSB
Use of RPAR and alternatives	EAB[c]	EAB
Performance evaluation of RPAR and alternatives		
Pest infestation and damage	ASIB	PSB
Comparative performance evaluation	ASIB	PSB
Use impact analysis (projected change in use)	EAB	EAB
Economic impact analysis		
Impact on production cost	EAB	EAB
Impact on volume produced	EAB	EAB
Impact on consumer prices	EAB	EAB
Aggregated economic impact	EAB	EAB
Limitations of analysis	EAB	EAB

[a] Animal Sciences and Index Branch.
[b] Plant Sciences Branch.
[c] Economic Analysis Branch.

Source: U.S. EPA (1977b).

procedure involves determining trade-offs between risks and benefits associated with each regulatory option and presenting them to the Deputy Assistant Administrator for Pesticide Programs. The integrity of the individual benefit and risk assessments is not compromised since they have already been completed. Regulatory action recommended on the basis of the benefit-risk analysis is presented.

Activity Flow

As shown in Figure 2.4, the first step in the RPAR activity flow is "core" data collection and validation, and the development of a use profile for the RPAR pesticide. The data gathered during this initial stage are augmented and used during the entire scientific inquiry of the RPAR process. OPP's Program Support Division provides core data from registrant files, other EPA files, and most importantly a worldwide literature search that is done under contract and produces a list of abstracts. The abstracts are reviewed by OPP—often by the project manager alone or with assistance from HED—and complete studies are obtained for selected abstracts. Studies that are relevant to the risk assessment are subjected to a validation procedure (see the section on Scientific Review in this chapter).

The next step is to determine routes of exposure. The project manager engages appropriate individuals from BFSD, HED, USDA, or outside contractors to determine routes of exposure on the basis of information about the chemistry and use of the compound. The early involvement of USDA, before the issuance of an RPAR notice, is important in order to begin fine tuning the mechanism for evaluating high-risk uses as opposed to low-risk uses.

While the project manager is coordinating the risk data validation procedure and evaluating the status of existing and needed data, risk and benefit assessment teams are formed and begin initial analyses. The risk analysis involves linking uses of the RPAR pesticide with hazards considered valid. The HED develops a preliminary exposure profile, i.e., a rough estimate of the number of people exposed to different dose rates, using the core data provided by the project manager (see Chapter 4, section on Exposure Analysis). The early presence of an exposure analysis enables a clear articulation of potential risk in the issuance of the RPAR notice and PD 1. It also creates the framework for formulating preliminary regulatory options to reduce exposure that can then be used as background material for subsequent benefit and risk analyses. The preliminary exposure profile and hazard data are used to provide the initial risk analysis transmitted to the project manager for use in developing PD 1.

The benefit analysis team begins the process of linking uses of the RPAR pesticide with economic and agricultural impacts attendant on the uses. This effort results in an initial examination of conditions that would be likely to result from cancellation, including use of alternative pesticides. The principal concern of a benefit analysis is assessment of the economic impacts a regulatory action would have on the pesticide users and on the consumers of the products of the users. The assessments are explicitly prohibited from considering any of the potential economic impacts a regulatory decision might have on pesticide manufacturers (U.S. EPA 1976: Appendix II). From the initial analysis, a plan of work is developed that will be shared with the risk analysis team and will be critical in selecting uses for in-depth analysis.

The project manager, taking into consideration uses, potential exposure, and toxicity data, drafts PD 1 or the statement of presumptive risk. If the risk criteria are reached or exceeded, an RPAR is issued. The RPAR notice should specify the extent to which critical information regarding exposure is unavailable, and requests should be made for this specific information. At the same time, additional data required for more definitive assessment of benefits and risks are identified and steps to acquire them are initiated.

Following the RPAR notice, the RPAR team determines the uses of the pesticide to be analyzed in depth and develops a range of draft regulatory options. The determination of which uses to analyze in depth depends significantly upon data supplied by the USDA/EPA benefit assessment team.

The benefit assessment team elaborates upon its initial estimate of alternative pesticides and the new use patterns that would result from the regulatory options that have been analyzed. The estimation of new use patterns is conveyed to the project manager and to the risk team. The risk team continues to validate or modify its initial risk assessment document and begins an assessment of the risks associated with alternative pesticides that would be likely to be used if a particular regulatory option regarding the RPAR pesticide were chosen. Meanwhile the project manager asks HED to conduct an analysis of rebuttals using HED staff and the CAG or contractors. Relevant information from this process is fed into the risk assessment. The rebuttal analysis and the decision as to whether the risk criteria have been rebutted are presented in PD 2.

The assessment of risks associated with current use of the RPAR compound is expanded by HED to include a comparison with risks from alternative pesticides that would be brought into use by the regulatory options being considered. Concurrently, the benefits team completes its assessment of economic impacts that would be expected to result from the previously formulated regulatory options.

The project manager next reviews the risk and benefit analyses to determine whether they can be used to describe the benefit-risk trade-offs associated with each regulatory option. A final group of regulatory options is then chosen, on the basis of the ability of changes in use patterns or use conditions to reduce the risks. The project manager, in consultation with the RPAR team, writes PD 3, which is a synthesis of the risk and benefit analyses. It describes and documents the risks and benefits associated with each regulatory option, and demonstrates the trade-offs between risks and benefits and the trade-offs among risks when alternative options are considered. When possible, the relevant trade-offs are displayed in a matrix, in which economic impacts of each option are presented in dollar terms and risks are presented in terms of numbers of anticipated morbidity or mortality incidences. For a more detailed discussion of OPP's current methodology for comparing risks and benefits see Chapter 6.

Once PD 3 is developed and approved, the proposed regulatory determination is drafted and sent to USDA and the SAP for external review.

SCIENTIFIC REVIEW

There is a consensus within EPA on the need for scientific review of the data base and positions formulated at the various steps in the RPAR process. There are several points in the process at which such review occurs. These reviews can be internal or external. Some are required by law, others have been created by EPA for the RPAR procedure, and still others are imposed by outside interests.

The first scientific review, which occurs before the RPAR notice is issued, involves only the risk data. The data base that is collected from the worldwide literature search to support PD 1 is subjected to a validation procedure. Validation is coordinated through the project manager and done either by contract, by in-house EPA scientists, or by a combination of these. It involves an examination of the test methodology or protocol, consideration of whether the results support the conclusions, evaluation of the study's weaknesses and strengths, and a general review of the value of the study to the RPAR process. Where cancer is an issue, this review is performed by the CAG.

Once an RPAR is issued, a kind of *de facto* scientific review of the risk data and EPA's assessment of it can occur through the rebuttal process. Often, major manufacturers will subject the scientific studies on which EPA's RPAR determination is based to a very thorough review and at the same time will review EPA's use of the studies in coming to its conclusions. These rebuttals, in turn, must be analyzed and evaluated by the project manager and the RPAR team. Again, if cancer is an issue, CAG is involved in the review.

If the risk criteria are not rebutted, a draft position document (PD 2/3) is prepared with an appropriate benefit-risk evaluation and presented to the working group and the PCRC for their review (see the previous section on Administrative Responsibility in this chapter).

The final scientific reviews are required by FIFRA, as amended, and are performed by external bodies. These reviews occur when a tentative decision is made and a notice of regulatory intent is issued. The tentative decision and the supporting benefit-risk evaluation are submitted to the

USDA and the SAP. The USDA is expected to review the decision with respect to agricultural economics; the SAP reviews it with respect to human health and environmental factors.

NOTE

1. *Acute Toxicity*

(A) Hazard to Humans and Domestic Animals.

(1) Has an acute dermal LD_{50} of 40 mg/kg or less as formulated; or

(2) Has an acute dermal LD_{50} of 6 g/kg or less as diluted for use in the form of a mist or spray;

(3) Has an inhalation LC_{50} of 0.04 mg/liter or less as formulated.

(B) Hazard to Wildlife

(1) Occurs as a residue immediately following application in or on the feed of a mammalian species representative of the species likely to be exposed to such feed in amounts equivalent to the average daily intake of such representative species, at levels equal to or greater than the acute oral LD_{50} measured in mammalian test animals as specified in the Registration Guidelines.

(2) Occurs as a residue immediately following application in or on avian feed of an avian species, representative of the species likely to be exposed to such feed in amounts equivalent to the average daily intake of such representative species, at levels equal to or greater than the subacute dietary LC_{50} measured in avian test animals as specified in the Registration Guidelines.

(3) Results in a maximum calculated concentration following direct application to a 6-inch layer of water more than 1/2 the acute LC_{50} for aquatic organisms representative of the organisms likely to be exposed as measured on test animals specified in the Registration Guidelines.

Chronic Toxicity

(A) Induces oncogenic effects in experimental mammalian species or in man as a result of oral inhalation or dermal exposure; or induces mutagenic effects, as determined by multitest evidence.

(B) Produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety; or

(C) Can reasonably be anticipated to result in significant local, regional, or national population reductions in nontarget organisms, or fatality to members of endangered species.

Lack of Emergency Treatments Has no known antidotal, palliative, or first aid treatments for amelioration of toxic effects in man resulting from a single exposure.

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A

3 Selecting and Scheduling Compounds for Assessment

INTRODUCTION

Some 35,000 pesticide formulations are registered for use in this country. Many, perhaps most, of these pesticides are innocuous when used properly. Serious questions have been raised about a number of others, however, because they may present risks to public health and to the environment.

Recognizing these risks, Congress, in the FIFRA amendments of 1972, required EPA—OPP in particular—to review the registrations of all 35,000 compounds within 4 years. In the 1975 FIFRA amendments, this deadline was extended a year, and in 1978 all references to a deadline were eliminated. The funds authorized to carry out the provisions of FIFRA, as amended—including non-RPAR activities—hovered around $50 million from FY 1976 to FY 1978. In FY 1979 the authorization increased to $70 million. The OPP staff compromised approximately 450 members in early 1976, and had increased to about 700 by early 1979, but even these resources (funds and staff size) have proved inadequate to the task at hand. A single RPAR procedure—namely, that for chlorobenzilate—occupied an RPAR team of 13 OPP professionals for a significant part of their time for 3 years. The direct personpower costs associated with the chlorobenzilate RPAR have been estimated at $400,000 (F. Arnold, OPP, EPA, Washington, D.C., personal communication, 1979).

By early 1979 only seven RPAR procedures had been carried through to a final decision. A total of 27 compounds have entered the RPAR process

(Jellinek 1979). About 20 compounds are in pre-RPAR stages, and another 20 are being considered or have already been selected for pre-RPAR review (Pesticide & Toxic Chemical News 1978).

Considering the current slow rate of progress in the RPAR program, the criteria by which suspicious pesticides are selected for evaluation and the order in which they are considered are matters of first importance. Realistically, it will be many years before the list of pending reviews is exhausted. Therefore, those compounds that appear most likely to have the greatest adverse impacts on public health or the environment should be selected for RPAR review before those compounds that pose less of a threat. This chapter is devoted to selection procedures. In the first section, we describe the current procedures for determining which pesticides are subjected to the RPAR process, and in the second section we present the Committee's recommendations for improving the selection process. The third section recommends a procedure for determining when and how thoroughly substitute pesticides should be considered in the RPAR process.

CURRENT APPROACH

To facilitate the following discussion, it will be useful to distinguish between the *total pool* of pesticide registrations up for review, those formulations selected as *candidates* for the RPAR process, and those actually *chosen* for formal RPAR consideration. The total pool of registrations is the roughly 35,000 registered pesticide formulations that EPA is required to review under the 1972 amendments to FIFRA. The intent of this legislated review is to subject all previous registrations to the newly established standards of safety outlined in the amendments. RPAR candidates are selected from the pool of registered pesticides; compounds in this category are subjected to a pre-RPAR review to determine whether they meet or exceed the risk criteria set out in 40 CFR 162.11 (see Chapter 2). Finally, those compounds that will actually be subjected to the RPAR process are chosen from among the RPAR candidates on the basis of the results of the pre-RPAR review.

SELECTION OF CANDIDATE COMPOUNDS FOR PRE-RPAR REVIEW

The current rather informal procedure for identifying and scheduling candidate compounds for pre-RPAR review seems to be a function of several elements. Some of the selection and scheduling decisions are based on considerations internal to OPP. However, a significant number of the decisions are made in response to various external pressures.

Many of the initial RPAR candidates were simply inherited. When the administration of FIFRA was transferred from the USDA in 1970, EPA established—as a forerunner of the RPAR process—the Suspect Chemical Review (SCR) program (NRC 1978). As part of this program, OPP's Criteria and Evaluation Division (now HED) had responsibility for identifying potentially hazardous pesticides and developing a "suspect chemical" list (NRC 1978). The identification of suspect chemicals was based largely on information extracted from various scientific publications, especially the Mrak report (U.S. DHEW 1969), which provided a comprehensive literature review and an assessment of the environmental and human health implications of a number of pesticides (NRC 1978). The specific criteria for selecting suspect chemicals included production volume, chronic and acute toxicity, and environmental fate data, but the details of the review process were not widely and explicitly reported (NRC 1978). Furthermore, not all of the registered pesticide formulations were reviewed.

In 1975 the RPAR process replaced the SCR program, and most compounds on the suspect list were included on an initial list of RPAR candidates. Chlorobenzilate, for example, was judged to be carcinogenic in the Mrak report, was included in the SCR program's suspect chemical list, and was accepted as one of the original RPAR candidates when the SCR program was replaced by the RPAR procedure. (Chlorobenzilate was also one of the first candidate compounds actually inserted into the RPAR process.)

In addition to relying upon the previous work of the SCR program, OPP also identifies RPAR candidates through reviews of applications for registration or reregistration. It is this review mechanism that constitutes the internal element in the candidate selection decisions.

Finally, RPAR candidates are also identified as the result of referrals, that is, information sources external to OPP. Referrals can come from a wide variety of sources, including other branches of EPA, public interest groups (e.g., the EDF), the Congress, and even complaints by individuals (NRC 1978). Treflan, captan, and 2,4,5-T, for instance, became RPAR candidates as the result of such referrals (F. Arnold, OPP, EPA, Washington, D.C., personal communication, March 1979). Referrals, which introduce an external element into the selection process, are frequently accompanied by some form of public pressure on OPP to act quickly.

SELECTION OF COMPOUNDS FOR THE RPAR PROCESS

Once a compound becomes an RPAR candidate, the criteria for determining whether it should be subjected to the RPAR process are clear and scientific. These are the risk criteria described in Chapter 2. However, the procedures for determining the order in which the RPAR candidates receive attention or are inserted into the RPAR process (once it is determined that they exceed the risk criteria) are not clearly and explicitly defined.

In some instances, high priority is assigned to those candidate compounds that involve use patterns similar to the use patterns of compounds that have previously been selected for RPAR (F. Arnold, OPP, EPA, Washington, D.C., personal communication, March 1979). This selection criterion might be explained on the grounds that the risk-benefit analyses for such a compound are greatly facilitated if the analysts have had previous experience with the use patterns.

In other instances, high priority is assigned to compounds that have relatively high exposure potential (F. Arnold, OPP, EPA, Washington, D.C., personal communication, March 1979). The advantages of this selection criterion seem apparent: other things equal, the greater the potential exposure, the greater the potential risk to public health or the environment.

Finally, external pressures on OPP are also presumably influential in some instances in determining which RPAR candidates are assigned relatively high priority, either for further evaluation as RPAR candidates or for insertion into the RPAR process. The same pressures (such as those from environmentalists, news media, or perhaps from Congress) that originally focused OPP's attention on a specific compound obviously can also result in the assignment of high priority to such compounds.

EVALUATION

It is difficult to describe the identification and scheduling procedure in more detail, since the basis for these determinations has not been well documented and reported. Early reregistration reviews were fraught with difficulty because of the disarray of EPA's data files and the lack of data to satisfy current registration standards (NRC 1978). In fact, for a while in mid-1976, EPA's registration and reregistration programs came to a virtual standstill. The type of toxicity data required by the 1972 amendments to FIFRA is not available for most older registrations, and it would take an inordinate amount of time and resources to generate such information as carcinogenicity test data. Efforts by EPA to obtain these data have often resulted in unavoidably long delays in regulatory activity. Compounds are put in a "holding pattern" when significant data are unavailable, and no determination is made as to whether they should be put through the RPAR process. The question is whether similar delays will again arise in the future or whether data necessary for future RPAR assessments are now being generated.

Lacking a sufficiently defined and formalized internal system for identifying and ranking RPAR candidates, OPP may be more susceptible to external and even capricious influences. The lack of a logical, documented method of establishing priorities appears to be a critical weakness of this part of the RPAR process. It is sometimes suggested, for example, that OPP selects compounds for research and regulatory activity, not on the basis of a carefully reasoned decision, but on what the media uncover as the "pollutant of the week" (see Walsh 1978, for example).

A serious flaw in the current procedure is that those compounds that receive the most publicity or pressure-group attention may not necessarily be those that present the greatest public health or environmental hazards. The current procedure does not provide for a broad comparison of the hazards posed by the large number of registered pesticides. At the same time, outside pressures to regulate a specific compound rarely arise from careful evaluations of comparative risks of alternative pesticides. To the extent that external pressures are influential in determining the order in which OPP evaluates compounds, the consequence may well be that considerable resources are devoted to regulating minor, low-risk compounds while important high-risk ones remain unreviewed for periods longer than would otherwise be the case.

In an agency with limited resources, the process of deciding which activity will be the subject of a regulatory action must always be to some extent *ad hoc*. Nonetheless, the Committee believes that OPP has the potential to develop a more consistent scheduling policy by emphasizing the impact of the pesticide on human populations.

RECOMMENDATIONS FOR ESTABLISHING A PRELIMINARY RPAR QUEUE

An alternative to the current procedures for identifying and ranking compounds for in-depth evaluation is proposed in this section. It appears most important that a clear, openly documented method be established for this process. The process recommended here is an extension of the current internal OPP system of automatic RPAR "triggers" based on the risk criteria in 40 CFR 162.11, and it is designed to put somewhat more emphasis on exposure and to establish comparative rankings of compounds in a priority queue. By following this system for identifying and ranking RPAR compounds, EPA would shift initial emphasis from toxic effects (see Chapter 2) to allow greater weight to be placed on potential exposure of humans and other nontarget species (livestock, crops, and the natural biota). These modifications are designed to reduce the effects of haphazard and extraneous considerations that currently influence OPP's scheduling procedures, and to provide a workable scheme for a preliminary screening of all 35,000 registered formulations. The procedure is intended to ensure that compounds that present the greatest overall risk to human health and the environment are identified, given appropriate priority for a thorough benefit-risk assessment, and assigned the necessary resources to complete a review expeditiously.

The following discussion of the recommended process is phrased in terms of risks to human health. It should be understood, however, that the possibility of significant adverse environmental effects is implicitly taken into account in our recommended procedure, although, as noted in Chapter 1, the report focuses on public health.

The Committee recommends the establishment of a two-stage pre-RPAR selection and ranking system. The first stage concentrates on classifying compounds according to their acute or chronic toxicity. The second stage establishes a preliminary ranking that indicates the approximate order in which specific compounds are to be evaluated. Exposure is emphasized in the second stage. The initial assignment of priorities may be altered somewhat as the RPAR evaluations proceed; this possibility is discussed in the next section. Both stages are designed to employ the fragmentary and limited data that are likely to be available before a pesticide has been studied seriously. Thus, the resultant rankings are tentative, and many are likely to be altered as additional information accrues. The remainder of this section considers both the substantive aspects of the proposed ranking system and the procedural issue of making the recommendation operational.

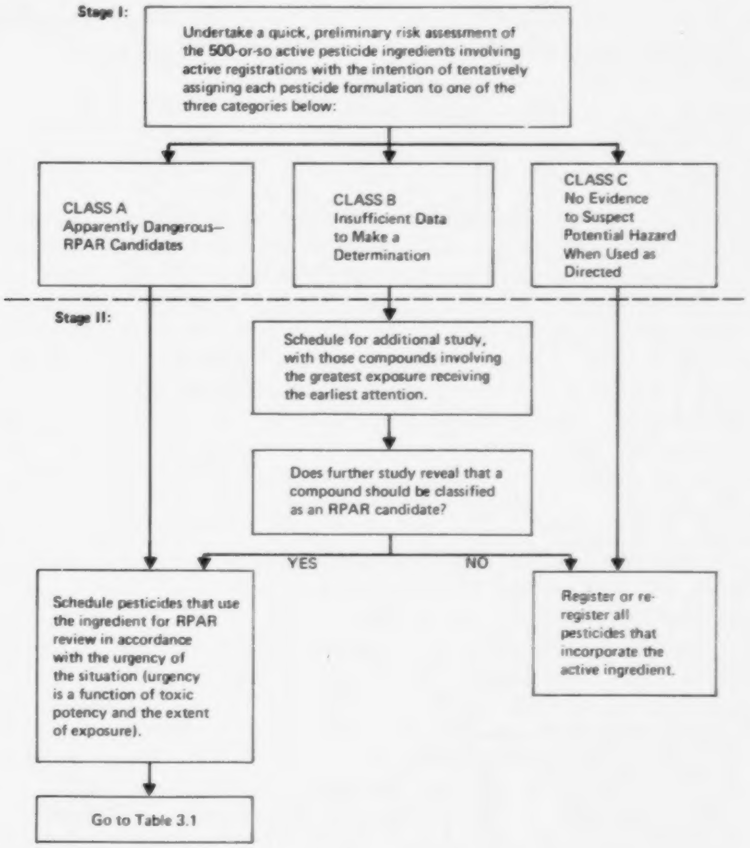
PRE-RPAR CLASSIFICATION OF COMPOUNDS

About 514 technical-grade ingredients are used in active registrations (Jellinek 1979). The first substantive step in ranking pesticides for review is to undertake a preliminary toxicity analysis of these 514 compounds (less those that have already been subjected to the generic standard process). The purpose of the preliminary toxicity analysis is to determine whether evidence suggestive of acute or chronic toxic activity that may present unique hazard exists. The preliminary analysis would be conducted according to the Agency's *Health Risk and Economic Impact Assessments of Suspected Carcinogens: Interim Procedures and Guidelines* (U.S. EPA 1976), and would be based only on data easily accessible in OPP or company files or in major scientific journals. It would not replace the worldwide literature search and the more thorough toxicity analysis conducted for the RPAR candidates (see Chapter 2); these would still be done, but at a later stage in the process. The rough, preliminary analysis is intended only to provide some indication of the compounds' inherent toxicity, not to serve as a substitute for later, more careful evaluation (if it is undertaken).

One problem recognized but not addressed by the PEAP Committee is that of impurities introduced into the active ingredients or the pesticide formulations by the complexities of industrial synthesis processes. Generally, the data on which preliminary toxicity analyses would be based do not include an assessment of impurities contained in commercial preparations. In fact, animal bioassays typically employ pure preparations, although in some instances it is the impurity in a pesticide formulation that poses the human health hazard. Thus, it is apparent that consideration must be given in the preliminary toxicity assessment to the possibility of potentially hazardous impurities entering commercial preparations.

On the basis of the preliminary toxicity assessment, each formulation should be placed in one of three classes: Class A, apparently a potential toxic hazard (an RPAR candidate); Class B, insufficient data to permit a reasonable judgment; and Class C, no evidence to suspect potential hazard when used as directed. This classification scheme, illustrated in Figure 3.1, is not fixed and irreversible, but will be subject to further review as additional pertinent data become available.

It should be noted at this point that, in addition to the acute and chronic toxicity criteria, a third type of risk can currently trigger an RPAR proceeding. This is the absence of an antidote or other emergency treatment for toxic effects in humans from a single exposure to a pesticide (see Chapter 2). Technically, this criterion alone, whether or not the acute toxicity criterion is met or exceeded, can trigger an RPAR proceeding. The Committee has not factored this third criterion into its preliminary selection and ranking scheme, but has chosen rather to concentrate on the acute and chronic toxicity criteria. It is expected that if information came to light during the selection and ranking procedures indicating that this third criterion may have been reached, the pesticide in question would be placed in Class A (an RPAR candidate) to be subsequently ranked within that grouping according to the scheme recommended in the next subsection.



Undertake a quick, preliminary risk assessment of the 500-or-so active pesticide ingredients involving active registrations with the intention of tentatively assigning each pesticide formulation to one of the three categories below:

CLASS A Apparently Dangerous—RPAR Candidates

CLASS B Insufficient Data to Make a Determination

CLASS C No Evidence to Suspect Potential Hazard When Used as Directed

Schedule for additional study, with those compounds involving the greatest exposure receiving the earliest attention.

Does further study reveal that a compound should be classified as an RPAR candidate?

Schedule pesticides that use the ingredient for RPAR review in accordance with the urgency of the situation (urgency is a function of toxic potency and the extent of exposure).

Register or re-register all pesticides that incorporate the active ingredient.

Go to Table 3.1

FIGURE 3.1 Recommended process for selecting and ranking pesticide formulations for assessment (see text for discussion).

The compounds in Class C—which include those compounds of apparently low toxicity and for which effective antidotes are available—require no further consideration by OPP (unless, of course, new evidence reveals a classification error). Accordingly, all currently active registrations involving these compounds should be renewed forthwith.

In contrast, the Class A and B compounds do require further attention. However, since there may be hundreds of compounds in these two categories, the order in which they are considered is especially important. We now turn to this issue.

PRE-RPAR RANKING OF COMPOUNDS

Class B Compounds

Since OPP can devote resources to only a few compounds at a time, it is necessary to rank Class A and B compounds in some order of priority. Class B compounds require further study to determine whether they pose problems of acute or chronic toxicity. The order in which these compounds receive attention should be directly related to their exposure potential. Other things being equal, those compounds to which many people (or many members of other significant nontarget species) are likely to be exposed should be assigned highest priority for further study. Compounds that are little used should be assigned relatively low priorities, unless there is some evidence suggestive of high toxic activity. Efforts should then be initiated to acquire the preliminary data needed to reclassify these compounds, beginning with those with the greatest exposure potential. When a compound has been reclassified, it either takes its place in the Class A list or is eliminated from further consideration, as a Class C compound.

Much of the work necessary to rank the Class B compounds (and probably the Class A compounds as well) has already been completed; OPP recently classified all 514 actively registered technical-grade ingredients as compounds of "major," "average," or "minor" significance (Jellinek 1979). The criteria for judging significance are production volume, numbers of registered products, residue tolerances issued, and volume and type of use. According to these criteria, only about 65 compounds are of major significance. Another 120 compounds are considered of average importance, and some 300 technical-grade ingredients are of minor significance. In accordance with these designations, the compounds in Class B that are of major significance would be the first to receive closer scrutiny in order to more clearly define the risks. If further testing is needed, OPP would probably have to seek the assistance of a research agency such as the National Cancer Institute, contract with a private testing laboratory, or require the testing of a registrant. (Prior to 1978, FEPCA did not give EPA the right to require additional testing by a registrant. However, as part of the 1978 revision of the standards for data sharing among applicants, EPA now has the power to require the submission of additional data that EPA feels are necessary to support a continued registration.) Attention would be directed next toward the Class B compounds in the average-significance category, and finally toward those whose significance is considered minor. Of course, it may be desirable to further order the Class B compounds within each of these three groups of significance. The main steps in this procedure recommended for dealing with Class B compounds are illustrated in Figure 3.1.

Class A Compounds

The Class A compounds are the RPAR candidates. OPP must determine which of these compounds (or the products in which they appear) reach or exceed the risk criteria set forth in 40 CFR 162.11. Those compounds identified as reaching or exceeding the risk criteria will be subjected to the RPAR process. According to the Committee's recommended procedure, the order in which these compounds (or the pesticides that contain them) should be examined more closely would be based on a preliminary risk assessment that accounts, in a rough fashion, for both potential exposure of human populations (or other nontarget species) and a compound's toxicity. That is, the preliminary risk assessment should consist of both a preliminary toxicity analysis and a preliminary exposure assessment. The preliminary toxicity analysis has already been discussed in the section on Pre-RPAR Classification of Compounds.

The purpose of the preliminary exposure analysis would be to identify those active ingredients to which significant numbers of people are exposed. Such exposures may occur either through persistence of residual quantities of pesticides in the food supply, or by contamination of water supplies or other environmental media. Briefer but more intense exposures may also occur during the manufacture, transport, and application of the pesticide formulation. To the extent permitted by existing, easily accessible data, both the amount of active ingredient that is likely to reach a typically exposed person in a given population and the number of people exposed to each dosage should be taken into account in this preliminary survey. The key factors in this accounting should be the chemical's environmental chemistry and the use patterns of the major products in which the active ingredient appears. As noted in the discussion of Class B compounds, OPP has already completed a substantial part of the work required for this preliminary exposure analysis and, thus, for the preliminary risk assessment.

The preliminary risk analyses should be used in ranking the Class A compounds. The preliminary ordering should take into account both the compound's exposure potential and its toxicity. Accordingly, highly toxic compounds with relatively high exposure potential should be assigned high priority and considered first, whereas weakly toxic, low-exposure compounds should be classified as low priority and considered last. Assignment of these priorities would necessitate a number of difficult and arbitrary decisions. It is not obvious, for example, how to order pesticides posing mainly environmental hazards relative to those likely to impair human health. The current practice of placing the greatest weight on human health hazards should probably be continued until such comparisons can be made more soundly than at present. Nevertheless, whatever ranking system emerges from these choices will involve less arbitrariness than the current selection and scheduling procedure. More important, the suggested ranking system would enhance greatly the likelihood that OPP's limited resources will be devoted systematically to regulating those compounds posing the greatest hazards to human health and the environment. Although the ranking system would become a subject of controversy, it would serve an important function by broadening the preliminary screening to include all active ingredients and by reducing the influence of unwarranted pressure on OPP's decisions.

The procedure described above determines the approximate order in which Class A compounds should receive further consideration from OPP. The ordering should not be regarded as fixed and irreversible: it would no doubt be revised as new data become available. Moreover, in order to reach correct RPAR decisions on specific compounds, it would sometimes be necessary to promote certain other pesticides to a higher position on the priority list. The latter possibility involves a number of complexities that are considered below. First, however, we discuss briefly one possible procedure for undertaking the preliminary risk screening discussed in this section.

CONDUCTING THE PRELIMINARY RISK SCREENING

In operation, the preliminary review, classification, and ranking shown in Figure 3.1 could be performed by a group of outside experts. Relying upon outside experts for an independent review and ranking would avoid placing significant new demands on OPP personnel and would enable OPP to enlist the skills of specialists not on its full-time staff.

A review system similar to that used by the National Library of Medicine (NLM) in its Toxicology Data Bank program might be used. In that program, an outside review committee is appointed, and each member is given data summaries for 10–15 chemicals. The summaries are supplied in computer format by the NLM through a contractor. Each committee member reviews the data on his or her assigned compounds for completeness and accuracy and is responsible for evaluating the data when the committee meets. In fact, the NLM has already reviewed many pesticides.

In this same spirit, OPP could establish a pesticide screening committee consisting of about a dozen consultants including toxicologists, pharmacologists, oncologists, and agricultural economists. The committee would have two functions and would be disbanded when those functions had been discharged. The first would be to classify the 500-odd active ingredients used in pesticide formulations into the three classes described earlier: Class A—apparently a potential toxic hazard (an RPAR candidate); Class B—insufficent data to permit a reasonable judgment; and Class C—no evidence to suspect potential hazard when used as directed. The second function would be to rank the Class A ingredients in order of importance.

It is visualized that such a committee would meet approximately one day a month and could be expected to classify active ingredients at the rate of about 10 at each session. The procedure envisioned is roughly as follows: At the first meeting or two the committee would have available the list of actively registered technical-grade ingredients and limited information about them, including the classifications already established into ingredients of "major," "average," or "minor" significance. On the basis of this information the committee would decide on the order in which ingredients are to be taken up for classification; ingredients of major significance that appear likely to be toxic on the basis of readily available information would be dealt with first and those of minor significance that are judged likely to be innocuous would be placed at the bottom of the list. Then the work would begin.

The classifications are to be based on information already available in EPA files, in published literature, in the NLM's Toxicology Data Bank and similar sources, and especially in the accumulated knowledge of the members of the committee. Obviously, the accuracy of the preliminary risk assessments and subsequent ranking of compounds will depend significantly on the quality of the data available and would be subject to modification as later data came to light. Each of the ingredients would be assigned to one or two committee members, who would be responsible for reviewing the sources of information and for reporting a digest of the information to the committee, with a recommended classification. The entire committee would then consider the evidence reported and arrive at a classification. Subsequent consideration would then differ depending on the class in question.

Class C ingredients do not require further consideration unless information indicating adverse affects on public health or the environment should come to light at a later date. Class B ingredients do require further work. When the committee assigns a chemical to this class, it should specify the minimal information it would need in order to reclassify it into one of the other classes. Then OPP should attempt to acquire the requisite information, and when it is obtained, the chemical should be returned to the committee's agenda for reclassification. Class A compounds are the candidates for possible RPAR proceedings and the committee should assign a priority rank to this list according to the procedures recommended earlier.

By the time the committee has been operating in this manner for half a year, an agenda of some 50–60 Class A ingredients will have been accumulated, all of them considered to be seriously toxic and to have the potential for widespread exposure. This agenda could then serve to schedule the more thorough reviews needed to determine whether pesticides incorporating that ingredient should be registered or reregistered, or whether the RPAR risk criteria set forth in 40 CFR 162.11 have been tripped.

MODIFICATIONS TO THE PRELIMINARY RANKING: THE ROLE OF ALTERNATIVE PESTICIDES

Once the tentative rankings have been completed, OPP should consider the compounds in order of priority. First, the pre-RPAR review would be conducted on the top-priority compounds to determine whether to initiate an RPAR proceeding. After an RPAR proceeding is begun, it will sometimes become necessary to promote some of the lower priority compounds (or at least some of their uses) to the front of the RPAR queue. The reasons and procedures for making such modifications to the initial priority queue are described in this section and presented in Table 3.1.

THE PROBLEM

The purpose of the benefit-risk assessments is to determine, for each use of an RPAR pesticide, how various regulatory options are likely to influence the level of risks and benefits arising from pest control activities. The public health, environmental, and economic effects of any regulation depend not only on the extent to which the regulation changes the use of the pesticide in question, but also on the changes it induces in alternative methods of pest control and in the public health, environmental, and economic effects of the alternative control measures. It is quite

TABLE 3.1 Decision Sequence for Uses of the RPAR Pesticide for Which Class A or B Pesticides Are Substitutes

Step	Assumption	Result of Analysis on Initiating Compound	Action on Initiating Compound[a]
1	No Class A or B substitutes will remain available	Risks > benefits	Disallow use or impose restrictions
		Benefits > risks	Go to Step 2
2	All Class A or B substitutes will remain available	Benefits > risks	Reregister for this use
		Risks > benefits	Go to Step 3
3	Obtain RPAR-type data on risks and benefits of major Class A substitute pesticides. Go to Step 4.		
4	Evaluate Class A substitutes sufficiently to form confident expectations as to which will be available. Assume Class B substitutes in use for 3 years or more will continue to be available.[b] Go to Step 5.		
5	Derived from Step 4	Benefits > risks	Reregister for this use
		Risks > benefits	Disallow for this use

[a] The only final decisions listed explicitly are "disallow" and "reregister." In many cases, restrictions on use (such as relabelling) may be feasible. A use subject to such restrictions should be regarded as a new use, and the same sequence of decisions should be followed.

[b] The 3-year time period is chosen for illustrative purposes and is intended to separate those compounds that have been in use long enough for some health or environmental problems to have surfaced. Further consideration may indicate that another measure is preferable.

possible for a regulation to have an adverse effect on public health if, for example, it induces more widespread use of a substitute chemical that is more toxic than the one being regulated. Even aside from this extreme possibility, a regulation may be unwarranted if it stimulates the use of alternative pesticides that are nearly as harmful to public health or the environment and that have substantially greater economic costs. To guard against these contingencies, two sorts of information are required: (1) the extents to which pesticide users are likely to resort to specific pest control alternatives, and (2) the effects of those alternatives on public health, the environment, and economic costs of protection. It is already routine to include in the analysis of any regulatory option an estimate of its effects on the use of alternative methods (chemical and biological) of pest control to which users are likely to resort. Such an estimate, however, will often be deficient because some of the regulatory options considered entail the use of pesticides that are awaiting RPAR proceedings, with results that cannot be foreseen. The systematic screening procedure recommended above will reduce the prevalence of this difficulty but cannot be expected to eliminate it entirely.

The second type of information mentioned above—relating to possible adverse effects of alternative methods of pest control—is not generated adequately under current procedures. At present, the RPAR team must make the best conjectures that it can about effects of substitute pesticides. The substitutes usually have not been subjected previously to systematic review.

The difficulties just described can present evaluators of a contemplated regulation with baffling perplexities. While the best information that can be obtained about the pesticide being evaluated may be at hand, it is usually the case that comparable information about alternative pesticides is lacking. Therefore, it is extremely difficult to estimate changes in benefits and risks that would result from the adoption of various regulatory options.

RECOMMENDATIONS

It follows from the forgoing discussion that assessment of the consequences of any regulatory option requires information about the public health, environmental, and economic effects of the regulated pesticides and comparable information about the effects of its principal alternatives. To generate this information for chemical alternatives, the Committee recommends that as soon as one of the high-priority compounds is assigned to the RPAR process, the RPAR team should identify all of the compound's uses and the alternative pesticides for each use. In some instances, restrictions associated with data, time, or budget may limit attention to a compound's major uses and the related alternative pesticides.

For any one use of the RPAR compound, there may or may not be chemical alternatives. For those uses for which there are no economically viable alternative pesticides, the RPAR evaluation should proceed as it currently does (amended by some of the Committee's recommendations in this and subsequent chapters). If the alternatives for a specific use are all Class C compounds (that is, presumed to be safe when used as directed), the same rule should apply: the RPAR evaluation for that use can proceed as at present, since it is realistic to assume that Class C compounds will continue to be available (unless the registrants voluntarily choose to withdraw them because they are not profitable).

If some of the alternative pesticides are in either Class A (RPAR candidates) or Class B (compounds for which there are insufficient data), the decision-making procedure becomes more complicated. A helpful tabular summary is presented in Table 3.1. It will be seen that the decision sequence is designed to minimize the amount of attention that has to be paid to substitute formulations.

Consider first those uses for which one or more of the alternatives are either Class A or Class B compounds (some may also be Class C compounds). In these cases, the RPAR evaluations for the initiating compound should first explore the possibility that the Class A or Class B alternatives will not continue to be available (i.e., that their registrations for the specific use in question will be cancelled). On Table 3.1, this is Step 1. If the risks of using the RPAR compound appear to outweigh the benefits when no Class A or B alternatives are available (and the benefits of using the RPAR compound are therefore at a maximum), the same state of affairs will prevail when one or more such alternatives *are* available. There is no need to explore further; the registration or reregistration for that use should be denied or severely restricted.

The scenario differs considerably if OPP determines that the benefits of a specific use of the RPAR compound outweigh the risks under the assumption that none of the Class A or B substitutes will be available (Table 3.1, Step 1, second possible result of RPAR analysis). The initiating compound should not necessarily be reregistered in this instance, since one or more of the Class A or Class B alternatives may be available and the advantages of the RPAR compound over the alternative may be insufficient to justify the additional risks entailed. To determine whether this possibility is, in fact, realistic, the benefit-risk estimates for the RPAR compound should next be recalculated under the assumption that all of the Class A or Class B alternatives for the use in question will be available (i.e., reregistered). In Table 3.1, this is Step 2. If, under this assumption, the RPAR compound continues to offer benefits in excess of the risks, then it should be reregistered for this specific use. In this instance, it is not important to have a well-founded judgment about the outcome of eventual RPAR proceedings against the Class A alternatives (or against those Class B alternatives that become Class A compounds).

If, however, in Step 2 the risks of continued use of the RPAR compound outweigh the benefits, it now becomes essential to have information about risks and benefits of the alternatives. If such information is not already available, the Class A alternatives will have to be pulled out of their places in the queue and given instant attention. They might be assigned to the same RPAR team, which will already be familiar with the economic and technical aspects of their use, or other teams may be

A

organized to develop the requisite data. The hard fact has to be faced that information ab[illegible] the alternatives is needed for a sound decision, and that decision[illegible] only be imperiled by waiting until the alternative compounds reach the top of the queue.

Thus, to obtain necessary information, it is necessary to issue "qualified" RPAR's for at least some of the Class A alternatives (Table 3.1, Step 3). These ancillary RPAR's are qualified in that they apply only to the use in question. For example, in connection with the chlorobenzilate RPAR, this recommendation could well lead to an auxiliary RPAR being issued for the use of dicofol as a citrus miticide, but not for dicofol's other uses. The ancillary RPAR's need be issued only for the crucial Class A alternatives, that is, those alternatives responsible for the ambiguity in the benefit-risk test for the initiating compound. In some instances all of the Class A alternatives will be crucial. However, in other instances some may be of such minor importance for the use in question that they would not reach or exceed the risk criteria in 40 CFR 162.11 and thus can be ignored. Clearly, the issuance of these additional RPAR's implies a selective reordering of the preliminary priority queue discussed above.

The auxiliary RPAR's will delay a final decision on the initiating compound. However, these delays are unavoidable if correct decisions are to be reached. Moreover, the length of the delays should be considerably shortened over time as the data base for all Class A compounds improves.

It becomes important to have a well-founded judgment about the availability of Class A and Class B alternatives if a use of the RPAR compound appears to entail risks in excess of the benefits when the alternatives are assumed to be available (i.e., at Step 2 in Table 3.1, second result of the RPAR analysis). The benefit-risk test implies different courses of action depending upon whether some or all of the alternatives continue to be available. Consequently, the question of continued availability of the crucial Class A alternatives—determined by conducting ancillary RPAR's—must be addressed before OPP can reach a correct decision on the initiating compound (Table 3.1, Step 4).

Finally, there remains only the situation in which (for a specific use) one or more of the alternatives to the initiating compound are Class B pesticides (that is, those pesticides for which the existing data do not permit their assignment into either Class A or Class C). The Class B alternatives should be incorporated into the benefit-risk evaluations of the initiating compound as follows. First, they should be divided into two subgroups: (1) those that have been in use for, say, 3 or more years, and (2) those that have been in use for less than 3 years. The dividing line is intended to separate those compounds that have been in use long enough for at least some health or environmental problems to have surfaced. The 3-year time period is an arbitrary suggestion; further consideration may indicate that some other period of time or a measure including the extent of use is preferable.

Next, the benefit-risk evaluations for the initiating compound should tentatively assume that those Class B alternatives that have been in use for the critical number of years will continue to be available (Table 3.1, Step 4). In contrast, it should be assumed that the recently registered Class B alternatives will not continue to be available unless there is at least some weak evidence to the contrary. The number of recently registered compounds that fall into Class B is likely to be rather small because of the testing requirements of the FIFRA legislation (as amended). As soon as the qualified RPAR evaluations for the crucial Class A alternatives are completed and the appropriate assumptions for the Class B alternatives are adopted, OPP can reach a sound final decision as to which toxic compounds to reregister for the use in question (Table 3.1, Step 5).

For present purposes, the relevant aspect of the preceding discussion, table, and earlier figure is the guidance they give concerning the order in which pesticides should be subjected to the RPAR procedure. To summarize, an initial ordering is established on the basis of preliminary information about the toxicity of active ingredients and the extent of human (and other) exposure to pesticides that incorporate them, with widely used compounds that contain the most toxic ingredients receiving the highest priority (Figure 3.1).

When any pesticide is reached on the priority list, substitutes for it in its major uses are identified. If any of these substitutes are in Class A or B and have not already been issued an RPAR, then the decision sequence summarized in Table 3.1 has to be followed for each such use. At Step 2, if it is reached, the pertinent substitute pesticides have to be pulled out of their low places in the queue and scheduled for early attention.

An important component of several steps is the determination of "Risks > Benefits" or vice versa. We have seen that such determinations require that the risks and benefits of alternative methods of pest control be taken into account, and therefore that adequate data on those alternatives be obtained by issuing qualified RPAR's or by other means.

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4 Risk Assessment

INTRODUCTION

The purpose of pesticide regulation in this country is to protect the human population, animals, useful vegetation, natural amenities of all sorts, and property from the "unreasonable adverse effects" of the use of chemical pesticides (PL 92-516, 1972). All pesticide regulations promulgated by EPA are intended to serve this purpose. Accordingly, a key component of the preparation of any regulation is an assessment of the dangers presented by the compound under review. If the assessment indicates there are substantial dangers, estimates are required of the extent to which they will be mitigated by various alternative restrictions and regulations that might be imposed. This chapter reviews the methods now employed by OPP in forming the requisite analyses and recommends a number of changes in those procedures.

Although in principle the risk assessment of any pesticide entails consideration of all the affected categories listed above, in practice, dangers to human health are currently EPA's predominant concern. Indeed, within the area of human health, OPP's attention is generally focused on possible oncological and mutagenic effects of suspect pesticides, since these are the most apparent adverse effects of the chemical pesticides now in widespread use and currently being introduced. The discussion in this chapter will therefore concentrate on the assessment of dangers to human health and particularly on the danger of inducing cancers. This narrow focus is dictated by time and resource constraints imposed on the study. It means that a number of important matters, in particular the assessment of environmental risks and eventual indirect effects on humans from long-term environmental effects, have been treated very briefly or not at all.

Determination of whether a pesticide poses a serious potential hazard is based on two considerations that are operationally separate. The first is the extent of exposure, that is, the number of people who may be expected to receive dosages of different levels and by different routes if the pesticide is used freely or if it is regulated in various possible ways. The second consideration is the pathological activity or toxicity of the pesticide, including the probability that a person exposed to specified doses by specified routes will suffer adverse effects of various degrees of severity, sometimes called the dose-response relationship. The analyses of these two aspects employ entirely different data and methods. They are conducted separately and are discussed separately below.

Assessment of the dangers to human health caused by the use of a pesticide is treated in the first major section of the chapter. The discussion is divided into three subsections, the first dealing with exposure analysis, the second with pathological activity, and the third with combining the previous two to obtain an overall assessment of risk. In each subsection the procedures currently used are reviewed critically and suggestions for improvement are made. The second major section of the chapter deals, more briefly, with the analysis of risks other than those to human health.

HAZARDS TO HUMAN HEALTH

EXPOSURE ANALYSIS

Current Approach

The purpose of OPP's exposure analysis is to determine in as quantitative a manner as possible the number of people exposed to a pesticide by various routes and the doses they receive. The analysis is developed on a use-by-use basis, and a special effort is made to understand how a particular pesticide is used and what human activities are associated with each use. For example, when an analysis is required for a pesticide with multiple uses, estimates are made of exposure by all routes for each use. The analysis includes a brief description of use practices, a summary of available data, and exposure estimates derived from the data.

The exposure analysis is used at two stages in the RPAR decision-making process (Severn 1978a):

(1) the initial decision to issue an RPAR rests in part on the likelihood of human exposure, so that a preliminary assessment of exposure (i.e., preliminary exposure profile) is needed at this stage; and

(2) once an RPAR has been issued, the final risk/benefit decision generally requires a more thorough analysis of exposure (the degree of completeness required depends in part on the toxic potency, extent of use, and magnitude of benefits to be derived from use of the pesticide in question, and is determined by the Project Manager and/or Working Group during the analysis leading to the final risk/benefit document—Position Document #3).

To date, there are no official agency guidelines for preparation of exposure analyses; however, a draft *Procedures Manual for Preparation of Human Exposure Analyses* (Severn 1978a) and other agency documents (e.g., internal memoranda) provide guidance until such guidelines become available.

Preliminary Exposure Profile A Preliminary Exposure Profile (PEP) is prepared for use in pre-RPAR activities. Essentially, the PEP is a rough estimate of the number of people exposed to different dose rates (for example, in terms of dose per hour of application) (Severn 1978a). Since few data on pesticide use are likely to be available at the pre-RPAR stage, the project manager maintains a core data base consisting of product label files, information from worldwide literature searches, and agency files of existing exposure information. The rough exposure estimates are determined by tabulating each use listed on the labels and comparing it with model exposure (that is, experimental application) situations, taking the compound's chemical and physical properties into consideration. The PEP thus lists each use indicated on the label along with an estimate of exposure from that use. As a compound proceeds through the RPAR process, additional data are sought to make possible a more detailed evaluation of the exposure situations with which the compound is associated.

Data for Exposure Analyses Ideally, a detailed exposure analysis for a pesticide would include estimates of exposure by all routes, both for the entire U.S. population and for particular subgroups that may have different levels of exposure, especially applicators and pickers. Therefore, data on numerous aspects of a particular pesticide are needed for precise estimation of the degree of human exposure associated with its use. OPP has identified several factors critical to the assessment of various exposure situations. The factors include group size; dose from each route of exposure; duration of exposure; statistical reliability of exposure estimates; and exposure to metabolites, by-products, impurities, and contaminants (Severn 1977a).

The worldwide computer literature survey made for each RPAR candidate pesticide identifies studies relevant to various aspects of the principal compound and its metabolites or degradation products (Severn 1977a). The studies serve as a primary source for many of the data needed to prepare a detailed exposure analysis of a given pesticide. Additional data sources include, among others, agency files, the USDA, the FDA, industry, user groups, the open literature, and universities.

Information on patterns and practices associated with the use of a pesticide serves as a basis for ranking use patterns according to potential for human exposure. Each use practice is thoroughly described, including all sites of application; formulations used at each site; application rates and dilutions; representative labels and packaging information; methods of mixing and loading; application techniques and schedules, including a description of apparatus and common practices during application, and the times and numbers of applications per year; number of applicators involved and their identity (farmers, commercial applicators, industrial users, and so on); extent of use (total acres treated and pounds used annually by crop and state); number of associated personnel involved in application (such as mixers, loaders, and flaggers); estimate of total hours of application activity; extent of use and kind of protective clothing; and percentage of each crop treated annually (Severn 1977a).

Data regarding patterns of exposure serve as a basis for estimating the amounts of a pesticide received through ingestion, inhalation, and dermal routes. Relevant information for exposure through ingestion includes data on food tolerances, residues, food consumption patterns, food processing and distribution practices, and drinking water surveys (Severn 1977a). The data come primarily from the open literature and Registration Division files of OPP. Estimates of food consumption patterns are based largely on nationwide averages (usually provided by USDA) and allow for variations in both geography and age (Severn 1977a). In addition, background data on food processing and distribution practices allow estimation of the extent to which foods consumed may be contaminated by residues of the pesticide.

Estimation of inhalation and dermal exposures is based on data from air monitoring, applicator practices, dynamics of application, and absorption of the compound (Severn 1977a). EPA surveys and the open literature are primary sources of available air monitoring data. Requisite data on applicators include numbers, extent of training, work schedules and practices, and protective clothing used. Information concerning the

TABLE 4.1 Sources of Data Used in Exposure Analyses of Selected Pesticides

Pesticide	Data	EPA Source
Treflan[a]	Air concentrations	Registrant
	Inhalation rate	Bioastronautics Data Book (1964)
	Duration of exposure	Doane Agriculture Station (1975) (applicators); USDA (field workers)
	Number of field workers	USDA
	Dermal exposure estimates	Wolfe et al. (1967); Hayes (1975)
Chlorobenzilate[b]	Number of applicators	USDA
	Inhalation/dermal exposure estimates	Wolfe et al. (1967)
	Average adult food consumption rates	USDA
	Residue data	Florida; USDA; EPA (limited)
Lindane[c]	Duration of exposure	EPA
	Inhalation/dermal exposure estimates	Wolfe et al. (1967)
	Food tolerances	EPA
	Food factors (commodity distribution)	EPA
	Extent of pesticide use	EPA

[a] Source: Severn (1977b).
[b] Source: Severn (1978b).
[c] Source: Donoso and Collier (1978).

dynamics of the application of a pesticide is based primarily on data concerning drift and transport near adjacent populations, runoff, persistence and reentry, and presence of particulates (Severn 1977a).

Human monitoring data come primarily from the open literature and EPA projects (e.g., the Human Monitoring Program). Relevant data include surveys of blood, urine, adipose tissue, and mother's milk (Severn 1977a). Also data from household surveys indicate the potential for exposure via pesticide-contaminated dust and home-use practices (Severn 1977a). Data used in selected exposure analyses for several pesticides are summarized with respect to type and source in Table 4.1.

Inhalation Exposure Estimates of respiratory exposure (i.e., via inhalation) are presented in terms of ambient air concentrations of the pesticide in the breathing zone of exposed persons (Severn 1978a).

Because air concentrations may vary widely, estimates of the likely range and mean of the concentrations are desirable. The physical state (vapor, aerosol, or particulate) of the pesticide is also noted. If sufficient data are available, time-weighted average concentrations are computed. Estimates of inhalation exposure for a given population are a function of estimates of ambient concentrations, duration of exposure, and number of people exposed. The Toxicology Branch of HED determines the rate of inhalation and the extent to which the pesticide penetrates and is absorbed into the lungs. Estimates of individual inhalation exposures are commonly derived either by measuring the concentration of the pesticide in samples of ambient air or by determining the amount of the pesticide actually trapped by the filter system of a respirator worn by a worker for a specified period of time (Hayes 1975). The first method requires calculation of breathing rates before actual inhalation doses can be determined. However, use of either approach appears to be determined more by the nature of available data (i.e., its quality and quantity) than by predetermined Agency guidelines.

Dermal Exposure Estimates of dermal exposure are presented in terms of milligrams of pesticide per hour that come into contact with the skin of exposed persons. The clothing worn by agricultural workers plays a critical role in the determination of dermal exposures (Severn 1978a). The extent to which pesticides that are deposited on skin are absorbed is determined by HED's Toxicology Branch. An important dermal exposure situation arises from reentry into areas previously treated with pesticides (Severn 1978a). It is difficult to predict quantitatively the actual dermal (and respiratory) exposure of, for example, orchard fruit pickers. Such exposure depends on the amount of residues remaining at the site, which relates directly to persistence and degradation characteristics of the pesticide in question. The Environmental Fate Branch of HED maintains a file of data on dislodgeable residues (mostly organophosphates) and other information on reentry. When an analysis requires an estimate of exposure during reentry, experts in particular geographical areas are usually consulted.

Ingestion Exposure The general approach to determining the amount of a pesticide ingested by humans in their diets is to multiply an estimate of the number of micrograms of the pesticide per kilogram of food in the various foodstuffs that may contain it by estimates of the amounts of those foods in a normal daily diet. The estimate of the amount of the pesticide per unit of a food is obtained in either of two ways. If there are actual measurements of pesticide residues in foods, those measurements are used. More frequently, the residue concentrations are too small to be measured by available analytical methods. In such cases, it is assumed that the foods contain the maximum amount of pesticide residue permitted by EPA (i.e., the tolerance level). The amounts of the foods contained in normal diets are derived from food consumption surveys conducted primarily by USDA, which are often adjusted for both geographic and age variations in consumption patterns.

Assumptions Data on many of the factors that are critical to the preparation of a detailed exposure analysis for a particular pesticide often are unavailable. In such cases, OPP either makes assumptions that it feels are necessary under the circumstances or, alternatively, derives estimates of exposure from data on other compounds that are used in similar patterns.

Assumptions made in preparing exposure analyses for the three pesticides displayed in Table 4.1 are summarized in Table 4.2. OPP's approach to estimating exposure of spray applicators to chlorobenzilate, for example, was based largely on the assumption that inhalation and dermal exposures vary the same way under different application conditions. The same assumption was used in the exposure analyses of Treflan (Severn 1977b) and Lindane (Donoso and Collier 1978). In the absence of data on actual applicator exposure to chlorobenzilate, probable estimates of both dermal and respiratory exposure were based on data for other pesticides used under conditions similar to those associated with chlorobenzilate (Severn 1978b). The data, as reported by Wolfe *et al.* (1967), consist of measured dermal and respiratory doses received by spray applicators while applying azinphosmethyl, DDT, dieldrin, malathion, and parathion. However, since the data reported by Wolfe *et al.* are based only on orchard spray conditions, OPP is initiating the development of models for other application situations (D. Severn, OPP, EPA, Washington, D.C., personal communication, 1978).

The assumption that 10 percent of the amount of a pesticide (in solution) that comes into contact with the skin is absorbed plays an important role in evaluation of dermal exposures. Although pesticides may be absorbed through the skin with varying efficiencies (Hayes 1975), the absorption rate of 10 percent has been used in several exposure analyses prepared by OPP (e.g., chlorobenzilate and Treflan; see Table 4.2). When, for example, information on protective clothing worn by agricultural workers is lacking, it is assumed that exposed workers wore short-sleeved shirts and long trousers but no hats or gloves (Severn 1978a). In this situation, estimates of dermal exposure are derived from existing data on measured skin deposition from a known spray

TABLE 4.2 Exposure Analysis Assumptions

Treflan

Air sampling data follow log-normal distribution
All inhaled NDPA[a] is retained, not exhaled
Ten percent of the amount of pesticide that comes into contact with the skin is absorbed
Field workers wear no protective clothing
Inhalation and dermal exposures vary the same way under different application conditions
Treflan will continue to be used indefinitely at about the current rate(s) of application

Chlorobenzilate

Occupational exposure of citrus pickers is less than that of spray applicators
Ten percent of the amount of pesticide that comes into contact with the skin is absorbed
Inhalation and dermal exposures vary the same way under different application conditions
Residues in treated commodities approach established tolerance levels
Inhalation per applicator-hour is the same as for other pesticides used in similar situations
Chlorobenzilate will continue to be used indefinitely at about the current rate(s) of application

Lindane

Residues in treated commodities approach established tolerance levels
Inhalation and dermal exposures vary the same way under different application conditions
Lindane will continue to be used indefinitely at about the current rate(s) of application

[a] Nitroso dipropylamine.

concentration of another pesticide (Severn 1978a). The dermal dose of other pesticides with similar spray characteristics can then be calculated from the spray concentration used. Since patterns of pesticide use are difficult to observe and enforce, there is, in many cases, a total absence of data on dermal and inhalation exposures during application. Although estimation of dermal effects attempts to incorporate both chemical and toxicological aspects of a particular compound, the 10 percent skin-absorption rate may be inaccurate by an order of magnitude. Studies are now under way to evaluate the roles played by skin and protective clothing as physical barriers in determining occupational exposures (D. Severn, OPP, EPA, Washington, D.C., personal communication, 1978).

For dietary exposures worst-case estimates are usually based on the assumption that residues exist in or on commodities at the limit of established tolerances. This assumption was used in both the Lindane and chlorobenzilate exposure analyses (see Table 4.2), but the availability of actual residue-monitoring data may permit more reliable estimates.

When estimates of daily exposure are converted to lifetime equivalents, OPP assumes that a pesticide will remain on the market and in use indefinitely. For respiratory and dermal exposures, which are usually occupational, exposure is assumed to occur over a typical number of work years for the number of days per year that a pesticide is used. For example, it was estimated that spray applicators were exposed to chlorobenzilate for 10–40 days per year (depending upon the number of applicators), over a 40-year work life (U.S. EPA 1978a). Dietary exposure was assumed to occur daily over a full 70-year lifetime.

Occasionally, there may be too few data available to permit a quantitative estimate of exposure. The 25,000–30,000 citrus pickers who may be exposed to chlorobenzilate represent a case in point. Here, OPP assumed that the pickers were less frequently exposed than the spray applicators (Severn 1978b), but no quantitative estimates were made.

In considering enforcement, OPP assumes that label restrictions will limit occupational exposure to some extent, and in this context, develops various regulatory options that may result in reduced levels of exposure. For example, the recommended regulatory option for chlorobenzilate includes requirements for specific types of clothing and respirators to be worn during application (U.S. EPA 1978a). A more detailed review of the chlorobenzilate exposure analysis is presented in Chapter 7.

Comments and Recommendations

In the Committee's judgment, OPP makes sensible and competent use of the often incomplete information available in performing its exposure analyses. The Committee does not recommend any far-reaching changes in OPP's general approach to exposure estimation, but there are a number of important changes that ought to be made in some of the detailed procedures followed and in the methods of presenting results.

Data Gathering and Use Exposure to a pesticide is not a simple mechanical matter. It depends on such properties of the pesticide as persistence, solubility, vapor pressure, adsorbability, partition coefficient, and thermodynamic characteristics. These properties influence the extent of vapor contamination, water contamination, biological availability, and persistence of residues. Estimates of exposure require information about all these chemical and physical properties of the pesticide and careful evaluation of their influence on the doses received through various routes by exposed populations. Estimates of exposure should take these considerations into account more extensively than now appears to be the case.

In estimating exposures, as in other phases of its work, OPP is constantly hampered by lack of adequate data, and is forced to resort to indirect and inaccurate methods in its effort to make plausible estimates.

A typical example is the use of the dermal and respiratory doses received by spray applicators while applying DDT, dieldrin, and several other compounds to estimate the doses received by chlorobenzilate applicators for whom no data exist. The valid use of such indirect evidence requires close and subtle familiarity with the pesticide under consideration, including its chemical, physical, and pathological properties, and details of the methods by which it is applied. Such familiarity can seldom be gleaned from the literature. The Committee therefore makes the following recommendation.

- *It should be routine practice for the members of the* EPA *staff team reviewing a pesticide to visit sites where it is applied, facilities where it is formulated and handled, and laboratories where it is studied, and on those visits to hold informal discussions with the people involved in day-to-day manufacture, handling, and use of the pesticide.*

Not only is there no substitute for this firsthand contact as a basis for informed judgment, but it has the further advantage of demonstrating to the people who will be affected by any future decision that their knowledge and views have been taken into account in the course of arriving at the decision. Agricultural experiment stations are particularly important sites for these visits and have the added advantage of often directing attention to useful publications of the stations or other sources that the usual literature indexes do not include.

Economic Life of a Pesticide For many pesticides, particularly those likely to induce cancers, the likelihood that an effect will eventualize is cumulative, so that estimates of lifetime exposures, rather than of rates of dosage during short periods, are relevant to risk assessments. As noted earlier in this chapter, the usual practice for making such estimates at present is to assume that if a pesticide is reregistered, it will continue to be used indefinitely at about current levels of application. In fact, the economic life of a pesticide or the length of time that it is expected to be bought and used is limited by (1) the rate of development of resistance or tolerance to it in the target pest, and (2) the introduction of more effective or economical alternative pesticides into the market. Thus, as do most tools, pesticides have a limited useful life.

Information on the economic life of pesticides should be included in all risk (and benefit) analyses of pesticides. Exposure, and hence risk, would generally be expected to drop to near zero as soon as a pesticide's economic life is spent and the pesticide is no longer used. Of course, there are always exceptions. For example, an environmentally persistent pesticide such as DDT may continue to present a potential for low-level exposure for a period ranging from a few months to more than 10 years beyond its economic life.

In order for OPP to make well-founded estimates of lifetime exposures to pesticides (as well as accurate benefit estimates), the Committee makes the following recommendation:

- OPP *should undertake or sponsor a study of the economic lives of pesticides and the factors that influence them. Estimates of both lifetime exposures and economic benefits should be based on periods of use consistent with the findings of the study.*

The Committee's best estimate on the basis of available information is that the use of a pesticide for specific pests has averaged about 10 years in a range of 2 to more than 34 years. (It should be recognized that the total economic lifetime of a pesticide encompasses all uses and therefore may be longer than the lifetime for a particular use.) When regulatory options are considered on a use-by-use basis, as they are in this report and in the OPP evaluations, the 10-year average figure, with its accompanying range, appears appropriate for estimating anticipated economic lifetimes until more reliable estimates become available. This figure, however, is rough and purely provisional and should be quickly superceded. Factors such as increasing testing costs and their effect on innovation in the pesticide industry may substantially alter estimates of the economic lives of pesticides in the future.

For pesticides that have already been on the market for a number of years, an educated guess based on expert opinion will have to suffice for the time being for estimating the additional average number of years those pesticides can be expected to remain on the market. For example, in Chapter 7, the Committee estimates that if reregistered, chlorobenzilate would continue in use for another 10 years beyond the more than 20 years it has already been used on citrus. In cases of this type, it should be assumed that, should registration of the pesticide be continued, additional exposure of the population and the resulting biological effects will not, on average, exceed the effects attributable to the additional years of use (unless persistence is known to be a problem).

Presenting Probable-Case Estimates and Confidence Limits There is a general tendency when estimates are uncertain, which is almost always the case, to adopt "conservative" estimates. If "conservative" means tending to err on the safe side, it must be pointed out that neither side is safe. On the one side, if a regulatory decision is predicated on erroneously low estimates of the number of people who would be exposed to injurious doses of a pesticide whose use is unrestricted, the decision will be biased toward inadequate restriction, with possible harmful consequences for public health. On the other side, if the estimate of exposure is excessively high, the resultant regulation is likely to impose economic costs that are disproportionate to the hazard averted, with a consequent waste of economic resources and of the goodwill on which EPA's effectiveness ultimately depends. The errors in question are by no means trivial; the phenomena leading to exposure and to adverse effects are so complex and so little understood, and the data relating to them are so fragmentary, that even best estimates may be substantially more than one order of magnitude in error.

The closest to a safe course in these circumstances is for the analysts to arrive at their best, unbiased (i.e., not intentionally conservative) judgment of the likely consequences of any regulatory option, and to present these estimates together with an indication of the range of uncertainty to the officials responsible for arriving at a decision. It is the responsibility of the officials, not the analysts, to weigh the relative seriousness of making errors on one side or the other. Those officials should be able to rely on the reports prepared for them to present fair, unbiased estimates from the facts and assumptions on which their decisions must rest.

Many of the estimates will be incorporated in public documents. Here, the same principle applies. That is, the public, including legislators and groups of interested citizens are all entitled to know the unvarnished truth: the best estimates that informed and thoughtful consideration can arrive at together with the ranges of uncertainty that surround them. Users of the estimates can then be relied upon to introduce whatever "conservative" biases they deem appropriate.

At present the position documents and supporting reports almost invariably violate this principle. Indications of ranges of uncertainty are rare. The position documents generally present as estimates of exposure the single, upper-limit, "worst-case" values for each exposed group. The qualifying considerations, probability factors, and ranges of uncertainty are not mentioned, leaving the estimated values unqualified by any assessment of their probability. Thus, the decision maker is not provided with information about how reasonable the worst-case values presented are nor with guidance for judging the levels of exposure that are likely to be the result of alternative regulatory options. The Committee's analysis of the exposure estimates for chlorobenzilate, given in Chapter 7, shows that in that instance the worst-case levels of exposure are highly improbable.

The use of tolerance levels for estimating the concentrations of pesticide residues in foods is an extreme instance of the same bias. When tolerance levels are imposed, food producers aim at concentrations that are safely below those levels, since if they aim at average concentrations too close to the permissible levels, much of their produce will be in violation. In practice, average concentrations of residues in foods are likely to be one or more orders of magnitude below the tolerance levels, so that basing dietary exposure estimates on tolerance levels generally overestimates such exposures by a factor of 10 or more.

It should be mentioned that worst-case estimates are not necessarily "conservative"—that is, they do not necessarily increase the likelihood of decisions that will protect health to the greatest extent possible in the circumstances. This perversity can arise when the difference between the worst-case estimates under unregulated use and under a contemplated regulation is smaller than the difference between the most probable results in the two situations. In such a situation the advantages of regulation may appear negligible or not worth the cost if worst-case estimates are used, while less biased estimates would disclose substantial probable reductions in exposure.

There is an additional reason for avoiding the practice of presenting only worst-case estimates in a risk appraisal: it interferes with the Administrator's exercise of judgment in choosing among alternatives. If a worst-case estimate of individual exposure is multiplied by a worst-case estimate of the number of people exposed, and the product is multiplied by a worst-case estimate of the carcinogenicity of the pesticide in question, then the result will be an unrealistically high estimate of the health costs of using the pesticide. Ideally, the Administrator would like to base decisions on the analyst's best judgment of the probable effects of adopting any option together with the analyst's judgment of the worst possible consequences consistent with the available data (i.e., the worst case).

For these reasons, the Committee makes the following recommendation:

- OPP *should continue to use its current procedures (with the modifications discussed above) for estimating exposures associated with various regulatory options. It should employ those procedures to derive estimated ranges of possible exposures under the different options. Those ranges should always be presented as a pair of numbers, one showing the exposure (or other aspect of risk) that is deemed most probable, and the other showing the maximum exposure (or component of risk) that is likely to be experienced in the absence of an implausible array of untoward circumstances, i.e., the worst case.*

A clear definition of "range" is required in order for this recommendation to be implemented intelligently. The Committee suggests that ranges be interpreted to mean that the probability that the true exposure is greater than the upper limit of the range and less than the lower limit is small but not negligible, perhaps about 5 percent. These confidence limits should, of course, take account of all sources of error and imprecision in the estimates, and should not be merely mechanical applications of statistical formulas.

ASSESSMENT OF CARCINOGENIC RISKS

The following discussion is devoted to the assessment of carcinogenic activity, partly because cancer appears to be the hazard of primary concern to EPA, and partly to permit an exploration of specific issues. Although the Committee has not explored other health hazards in as much detail, we believe that appraisals of other hazards to health have to overcome many of the same problems and should be approached by much the same methods.

Current Practice

The general procedures for assessing the risks to human health posed by suspected carcinogens are described in the Agency's *Health Risk and Economic Impact Assessments of Suspected Carcinogens: Interim Procedures and Guidelines* (U.S. EPA 1976, referred to throughout as the guidelines). The basic evaluative framework established by the guidelines has several important features.

The guidelines clearly state the Agency's basic philosophy regarding the regulation of suspected carcinogens. It is noted that " . . . in many areas risks cannot be eliminated completely without unacceptable social and economic consequences" (U.S. EPA 1976:21402–3). Accordingly, the guidelines establish, as the basic regulatory objective, the elimination or reduction of risks " . . . to the greatest extent possible consistent with the acceptability of the costs involved" (U.S. EPA 1976:21403). This regulatory philosophy—allowing for trade-offs between risks and benefits—is quite different from the one imposed upon the FDA by the Delaney Clause of the Pure Food and Drug Act.

The guidelines create a two-step decision-making process for the regulation of potential carcinogens. The first step in the process involves determining whether and to what extent a particular substance constitutes a cancer risk. The second step involves selecting the specific regulatory assessments are conducted as part of the first step in this regulatory sequence.

The guidelines identify two objectives that are to be addressed in assessing carcinogenic risks of suspect chemicals:

1. To evaluate the evidence concerning a particular agent and from this to judge whether the agent is a potential human carcinogen.
2. If it is, the next step is to judge the likely extent of its effect on public health, with specific reference to cancer, at current and anticipated levels of exposure.

The responsibility for making these judgments resides with EPA's CAG.

In connection with the first issue—whether a substance constitutes a cancer risk—the guidelines recognize the difficulties attendant on "proving" that an agent is a human carcinogen. Thus a substance is to be considered " . . . a presumptive cancer risk when it causes a statistically significant excess incidence of benign or malignant tumors in humans or animals" (U.S. EPA 1976:21403). The judgment is to be based upon a "weight-of-evidence" approach that relies upon a wide range of data sources, including human epidemiological studies, animal bioassay studies, and short-term *in vitro* tests. In general, the determination of whether a substance is a human carcinogen is to be based upon available information; the guidelines impose no requirements for the acquisition of new data (U.S. EPA 1976:21403).

The guidelines distinguish among several different types of evidence on the basis of quality and adequacy:

> The best evidence that an agent is a human carcinogen comes from epidemiological studies in conjunction with confirmatory animal tests. Substantial evidence is provided by animal tests that demonstrate the induction of malignant tumors in one or more species including benign tumors that are generally recognized as early stages of malignancies. Suggestive evidence includes the induction of only those nonlife shortening benign tumors which are generally accepted as not progressing to malignancy, and indirect tests of tumorigenic activity, such as mutagenicity, in-vitro cell transformation, and initiation-promotion skin tests in mice. Ancillary reasons that bear on judgments about carcinogenic potential, e.g., evidence from systematic studies that relate chemical structure to carcinogenicity should be included in the assessment. (U.S. EPA 1976:Appendix I, 21404)

With regard to the second issue—determining the extent of the cancer risks—the guidelines commit the Agency to quantitative risk extrapolations (U.S. EPA 1976:Appendix I, 21404). The extrapolations are to be based upon the best available evidence concerning exposure levels and are to be performed with a variety of risk extrapolation models, such as the linear nonthreshold model and the log-probit model (Crump *et al.* 1976, Hoel *et al.* 1975, Mantel and Bryan 1961). Moreover, the extrapolations must be done separately for all suitable experimental data and human epidemiological data. The guidelines recommend that the results be presented in terms of excess lifetime incidence, or average excess cancer rates. At the same time, the guidelines recognize that there are considerable uncertainties surrounding these risk analyses (see below), and accordingly emphasize that the extrapolation results should be interpreted only as a "warning signal" rather than as an actual indicator of excess cancer incidence.

Comments

The CAG typically mounts a well-informed and conscientious effort to meet the expectations of the guidelines. It evaluates the available evidence from bioassays in experimental animals and from epidemiological observations and weighs biochemical and toxicological information in assessing the carcinogenic activity of the pesticide under study. However, although the guidelines indicate that a "weight-of-evidence" approach is to be taken in judging data, precisely how this is done is unclear. Criteria for determining the weight of evidence are not stated in the guidelines and have not been thoroughly discussed elsewhere; consequently, the judgments appear to be made in an *ad hoc* manner without formal criteria.

It would be desirable for CAG to provide some formal discussion of its criteria for making weight-of-evidence judgments. These criteria should consider how CAG would proceed to arrive at a judgment where multiple sources and types of evidence are available. For example, how would evidence from a well-performed bioassay, with adequate numbers of experimental and control animals, that showed no carcinogenicity for a compound be compared and weighed against a far smaller study, perhaps with inadequate numbers of animals, that showed a strongly positive effect at comparable dose levels? How would strong evidence of mutagenicity or carcinogenicity in short-term tests *in vitro* be assessed in comparison to marginal studies showing no cancer excess in carcinogenesis bioassays *in vivo*? Would the weight of evidence fall on the side of the positive study, the more thorough study, or the study of animals *in vivo*?

When the available, technically adequate evidence is conflicting, the risk assessments reviewed by this Committee indicate a strong tendency for CAG to place most weight and credence on data that show the strongest carcinogenic responses. The tendency to err on the safe side appears to be a general CAG practice. To the extent that this is the policy of CAG it should be formally stated. Along these same lines, as noted earlier in this chapter, OPP also prefers to use exposure estimates that may err by indicating an excess in number and dosage of exposed individuals to estimates that may err by understating these variables. Estimates of exposure and evaluation of carcinogenesis should be specifically discussed to clarify how the weight-of-evidence judgment was achieved for each from the existing data. Finally, CAG also chooses extrapolation methods that, if they are in error, overestimate rather than underestimate risk.

In this way, estimates and extrapolations all are permitted to err but, it is hoped, in such a way that the error will always overstate the risk. The intent of this worst-case approach is to allow the assumption that estimated risk always exceeds real risk. Clearly, however, others judging the weight of evidence might arrive at different determinations of risk. Because weight-of-evidence judgments are inherently subjective, the CAG should explain (1) how such judgments were achieved in each specific case, and (2) its criteria for making such judgments in general.

The Committee found a more major problem having to do with EPA's use of CAG's numerical estimates of human cancer incidences. The Committee's difficulties stem from the belief that current understanding of carcinogenesis and related pathologies is not adequate to permit reliable extrapolations from animal experimentation and simpler assay systems to actual quantified hazards to human health (see Appendix A for more detailed support of this statement).

Adequately controlled and documented epidemiological data for relevant populations are rarely available, and human experimentation with suspected carcinogens *in vivo* is unthinkable. Consequently, experimental data from bioassays in animals must be relied upon in most cases. Uncertainty and error from at least three sources infiltrate quantitative estimates of human cancer risk from animal data (see Appendix A). First, pathological evaluations upon which an estimate of excess tumors in test groups are based are to a certain extent subjective, and are often controversial (for example, see Pesticide & Toxic Chemical News 1978 and 1979). Moreover, such evaluations are not presented with confidence intervals. Second, at least two extrapolations of inadequately tested reliability must generally be applied to bioassay data to derive estimates of human cancer incidence. Extrapolations must be made between species—i.e., from experimental animals to humans—and extrapolations must be made from experimentally used dose levels, which are generally quite high, to actual dose levels encountered by humans. (The determinations of heptachlor's pathological activity were based upon experiments in which mice were given doses some 13,000 times as great as the doses to which humans were being subjected.) In some cases, a further extrapolation must be made to compensate for differences in the route of exposure between experimental animals in bioassay studies and actual routes of human exposure. Finally, present methods do not include means for evaluating the influences of several critical determinants of human cancer, such as differences in human susceptibility and additive or synergistic effects operative in the human population. Consequently, the Committee believes that inferences drawn by means of current extrapolation methods lack scientific justification, particularly when they are used without the support of epidemiological data and when they are used as a general method for all suspected carcinogens. Moreover, at a practical level, they have been insufficiently validated by past experience.

Although there is obvious value to developing and verifying methods for extrapolating from observed experimental tumor responses in animals to effects at low doses in humans, current methods present significant and controversial scientific problems (see IRLG 1979). Ultimately, when there is greater insight into the mechanism of carcinogenesis and methods are available for integrating variations in individual human susceptibility and the effects of exposures to other carcinogens and co-carcinogens, extrapolations based on this insight may provide reliable estimates of human cancer incidences from the use of a compound. With the present state of knowledge, the results of bioassays and short-term tests may be useful as comparative measures (to compare one carcinogen to another) of anticipated effects of various carcinogens at human exposure levels, but extrapolation techniques are not yet sufficiently precise or well-founded to allow us to make credible quantitative extrapolations about the anticipated frequency with which cancers will be induced in the human population by exposure to the estimated doses of the pesticide. Most important is the possibility that because of unconsidered factors, the worst-case extrapolation could actually be an underestimate.

The members of CAG are in a difficult position. They interpret their responsibilities as requiring them to present numerical estimates of the effect of using the pesticide under review on the incidence of cancer in the exposed population. They are aware that current scientific knowledge does not justify such estimates *per se*, and they consistently qualify their reports accordingly (see Appendix A). Nevertheless, they are required to present numerical estimates and they produce a product buttressed by impressive statistical and mathematical analyses. Whereas CAG arrives at these estimates with appropriate constraints and reservations placed on their final result, the provision of a sophisticated quantitative estimate of human cancers provides a high potential for misinterpretation because the estimates may be used without the required attention to the inherent constraints. In fact, in this Committee's opinion, the convenience of comparing risks as estimated numbers of human cancers to benefits in dollars makes it highly unlikely that misuse of extrapolation results can be avoided.

In the view of this Committee, CAG should be more aware that users are so hungry for numbers that quantitative estimates, once presented, take on a life and authority of their own, despite all the reservations that CAG may attach to them. In the context of EPA's procedures, CAG estimates are incorporated into benefit-risk estimates upon which choices among regulatory options are based. To be sure, the estimates themselves are accompanied routinely by warnings that they are subject to error. The Committee, however, did not encounter any document that conveyed the impression that the risk estimates could well be in error by as much as 1,000–10,000 percent. Yet the methods of extrapolation used by CAG, which reflect the best current scientific understanding, are subject to uncertainties of that order of magnitude or greater (see Appendix A). Such risk estimates are quite unsuited to comparisons with benefit estimates that, crude as they are, can be trusted well within one order of magnitude.

Recommendations

For the preceding reasons the Committee recommends that EPA not require CAG to estimate the numbers of people who would be expected to contract cancer or other diseases as a consequence of pesticide (or other chemical) use under various regulatory options. At the same time, the Committee recognizes that the Administrator needs some quantitative indication of the danger posed by a pesticide that he or she is called upon to regulate. In these circumstances the Committee believes that the best assistance scientific advisors can offer the Administrator is to provide intelligible information concerning the experimental and epidemiological evidence upon which a judgment of risk is to be based.

With respect to judging whether a compound is a carcinogen, the conservative position appears to be to accept the induction of tumors under laboratory conditions as presumptive evidence that a compound has the potential to act as a carcinogen or mutagen in humans. The Committee accepts that position. Beyond that, since compounds vary enormously in their degrees of carcinogenicity or mutagenicity, the Administrator is responsible for judging whether a specific pesticide imposes a risk great enough that its use might have an *unreasonable* adverse effect on the health of the exposed population. The judgment usually must be based on experimental indications, primarily from bioassays using small rodents, of the pathological activity of the compound.

Although the Committee believes experimental findings do not permit sound numerical estimates of potential human cancer incidences, experimental findings often do permit placing a compound on a scale of probable *relative* human carcinogenic activity, along with other compounds for which comparable experimental results are available. One approach to estimating the relative carcinogenicity of compounds to humans is recommended in the next subsection. The Administrator can thus be informed of how the carcinogenic activity of the compound under study is likely to compare with that of other compounds with which he or she may be more familiar and which have been judged to be suitable or unsuitable for use. (Such comparisons are useful to decision makers only in circumstances where the compound under review yields benefits comparable to those of the compound to which it is being compared. This concept is discussed further in Chapter 6.)

The Carcinogenic Activity Indicator The remainder of this subsection is devoted to a procedure by which the Committee feels compounds can be placed on a scale of relative human carcinogenic activity based on animal bioassay data. Expressions of the relative carcinogenic potentials of compounds have been described previously by means of a number of "potency indexes" (for example, see Meselson and Russell 1977). The following presentation is based on a potency index type concept, recommending the use of a Carcinogenic Activity Indicator (CAI) developed by the Committee and defined as:

$$\text{CAI} = \frac{\text{Excess percentage of subjects in which tumors are observed}}{\text{Lifetime dose (m moles/kg of body weight)}}.$$

It is critical to understand at the outset that CAI's will be calculated for animals only, on the basis of bioassay data; estimates of the carcinogenic activity of a single compound in humans are never made. The procedure depends, rather, on *comparing* CAI values derived for different compounds in animals—under proper conditions—to provide indications of the *relative* carcinogenic potential of these same compounds in humans. (The assumptions that allow this use of CAI's are discussed in Appendix B.)

Table 4.3 presents experimentally derived CAI's for a number of compounds. The calculation of a CAI and the conditions under which the relative carcinogenicities of two or more compounds can be compared in experimental systems are described more fully in Appendixes B and C. A number of difficulties in the interpretation of CAI's should be made explicit here:

1. CAI's for a given compound derived from experiments with different species are likely to differ substantially. For example, the CAI's for chloroform ranged from 23.7 to 41.9 when mice were used, but measured only 1.59 in rats (see Table 4.3). Such differences in CAI's observed in two species of rodent make it clear that inferences about the CAI of the same compound in humans must rest upon a substantial ingredient of judgment.
2. For any single species, the observed CAI may be different for different routes of administration.
3. A CAI is derived from a single point on a dose-response curve by dividing the response by the dose. The CAI may therefore be expected to differ with different experimental doses. A dose-CAI curve for vinyl chloride, plotted from data in Table 4.3, is shown in Figure 4.1. Note that log-log scales are used. The observed CAI ranges from about 7.8 for a dose of 0.74 m moles/kg to 1,985 for a dose of 0.0037 m moles/kg.
4. The sample sizes used in many bioassays are so small that the observed values are subject to substantial statistical error. For instance, in a bioassay using 50 animals each in the test and control groups, a 15 percent excess incidence of tumors could be observed in the test group in about 1 experiment in 15 even if the chemical tested were innocuous, while no excess incidence might be observed for a dose of a tumorigenic chemical that on the average increased incidence by 18 percent.

All these limitations must be taken into account when CAI's are used to compare the carcinogenic potentials of different compounds. The comparisons will be most tenable when the experimentally observed CAI's being compared are derived from experiments conducted with the same species, using the same routes of administration, and administered in doses yielding approximately equivalent excess tumor incidences. Even then, due consideration must be given to experimental error. Note again that only animal CAI's derived from bioassay data are being compared; no extrapolations to humans have been made.

Table 4.3 is intended to be more suggestive than definitive, since the Committee's resources did not permit an adequate review of the literature. The CAI's shown were all computed from published experimental data. They show estimates of the percent of animals exposed to the compound listed that developed tumors as a result of the exposure in relation to the lifetime dose (in millimoles per kilogram of body weight) received by the animals in the experimental group. Table 4.3 suggests

TABLE 4.3 Experimentally Observed Carcinogenic Activity Indicators of Selected Carcinogens by Species and Route of Administration

Compound	CAI[a]	90 Percent Confidence	Sex	Feed or Air Concentration (ppm or mg/kg body weight)	Lifetime Dose (m mole/kg)	Percent Tumor Response[b]	Derived From
Mouse oral							
Aldrin	1.5	0-35.8	M	4 ppm	1.023	1.5	NCI (1978a)
	14.6	0-34.5	M	8 ppm	2.046	30	
	16.9	0-55.4	F	3 ppm	0.767	13	
Chlordane	3.1	0-11.5	M	5 ppm	1.11	3.4	Epstein (1976), IRDC (1973)
	14.5	11.8-16.1	M	25 ppm	5.55	80.3	
	6.9	5.3-7.9	M	50 ppm	11.1	76.7	
	11.3	9.0-13.3	F	25 ppm	5.55	62.7	
	6.0	4.7-7.1	F	50 ppm	11.1	66.7	
	3.8	0-8.2	M	29.9 ppm	6.81	25.7	NCI (1977a)
	6.2	4.2-7.0	M	56.2 ppm	12.80	79.2	
	0.95	0-4.6	F	30.1 ppm	6.86	6.5	
	5.0	3.6-5.8	F	63.8 ppm	14.53	72.3	
Chloro-benzilate	0.27	0.15-0.38	M	603 ppm	178	47.6	Innes et al. (1969)
	0.049	0.020-0.064	M	4231 ppm	1183	58.5	NCI (1978b)
	0.016	0-0.027	M	7846 ppm	2194	35.0	
	0.016	0-0.047	F	3200 ppm	895	14.7	
	0.004	0-0.022	F	5908 ppm	1652	6.7	
Chloroform	33.1	0-52.2	M	138 mg/kg	1.155	38.3	NCI (1976)
	41.9	35.7-41.9	M	277 mg/kg	2.318	97.1	
	40.3	31.4-45.0	F	238 mg/kg	1.992	80.2	
	23.7	20.1-24.7	F	477 mg/kg	3.992	94.6	
Dicofol	0.86	0.25-1.16	M	264 ppm	64.84	55.7	NCI (1978c)
	0.55	0.30-0.66	M	528 ppm	129.68	71.2	
Dieldrin	16.3	0-60.1	M	2.5 ppm	0.6126	10	NCI (1978a)
	16.3	0-36.8	M	5 ppm	1.225	20	

	21.2	0-60.7	F	2.5 ppm	0.6126	13	
	3.3	0-24.3	F	5 ppm	1.225	4	
Endrin	39.8	0-70.9	M	3.2 ppm	0.784	31.2	NCI (1979)
Ethylene	0.0847	0-0.326	M	13.3 g/kg	70.8	6	Olson et al.
dibromide	0.0143	0-0.136	M	26.3 g/kg	140	2	(1973)
	0.0565	0-0.297	F	13.3 g/kg	70.8	4	
	0.0143	0-0.136	F	26.3 g/kg	140	2	
Heptachlor	19.4	14.3-22.9	M	10 ppm	3.25	62.9	NCI (1977b)
	21.3	18.0-24.0	F	10 ppm	3.25	69.3	
Rat oral							
Chloroform	1.59	0-56.8	M	90 mg/kg	0.753	1.2	NCI (1976)
Endrin	13.6	0-87.3	M	5 ppm	0.588	8	NCI (1979)
Ethylene	3.29	3.03-3.34	M	5.6 g/kg	29.8	98	Olson et al.
dibromide	1.04	0.78-1.24	M	11.2 g/kg	59.6	62	(1973)
	1.52	0.83-2.05	F	5.6 g/kg	29.8	45.3	
	0.41	0.03-0.72	F	11.2 g/kg	59.6	24.2	
Lindane	0.377	0-1.41	M	236 ppm	36.3	13.7	NCI (1977c)
	0.0923	0-0.644	M	472 ppm	72.7	6.7	
Rat inhalation[c]							
Vinyl	1985.5	0-5247		50 ppm	0.00371	7.4	U.S. EPA
chloride	1005.9	266.2-1755.3		250 ppm	0.0186	18.7	(1975)
	810.0	389.2-1209		500 ppm	0.0371	30.1	
	263.2	171-337.8		2500 ppm	0.186	49.0	
	103.6	69-133.7		6000 ppm	0.445	46.1	
	78.3	58.4-94.5		10^4 ppm	0.74	57.9	

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[a] Carcinogenic Activity Indicator (CAI) equals "excess percentage of subjects in which tumors are observed" over "lifetime dose" (in m moles/kg body weight), with 90 percent confidence intervals. CAI calculations are based on primary tumors reported, not secondary. See text and Appendixes B and C for more detailed discussions of CAIs and how they and their confidence intervals are calculated.

[b] This column presents the excess probability of tumor incidence among test animals (p_x), using Abbott's formula, $p_x = 1 - [(1 - p_t)/(1 - p_c)]$, where p_t and p_c are the proportions of test animals and control animals, respectively, that contracted tumors.

[c] Male and female data were not reported separately; test groups included male and female subjects.

Note: This chart is intended as an example of CAIs for a few select compounds; it is not an exhaustive list of compounds, nor are all possible data used for the compounds selected. The best data available were used for calculating CAIs; it is possible that new and better data may provide more sound estimates in the future.

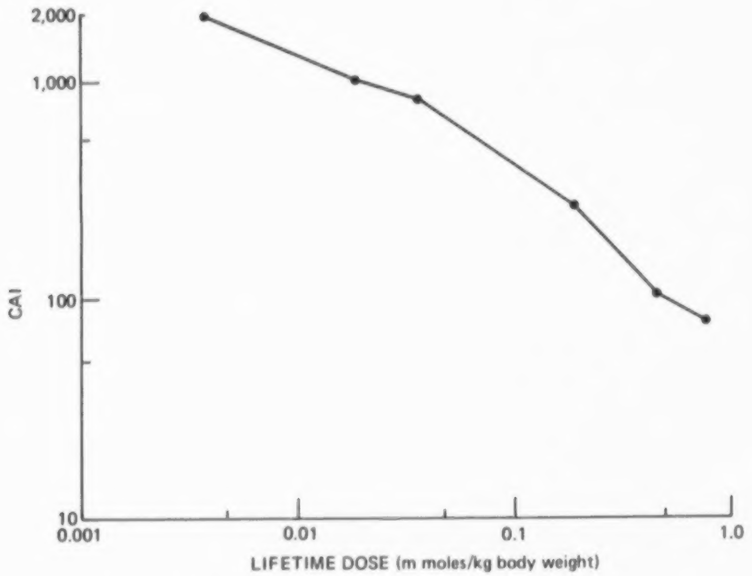

FIGURE 4.1 Relationship between CAI and dose for vinyl chloride. Source: Derived from Table 4.3.

that on the average for mice administered test compounds orally and demonstrating comparable tumor response levels, heptachlor is approximately 30 times as active a carcinogen as dicofol. This is because under similar experimental conditions a given number of moles of heptachlor per unit of body weight will have approximately 30 times as great an effect (on the basis of the data reviewed) on the probability of developing excess tumors as the same number of moles of dicofol. Similarly, using data from Innes *et al.* (1969), chlorobenzilate, when administered orally, is about one third as active as dicofol in inducing tumors in certain laboratory mice. The table therefore can serve as a scale against which the pathological activity of any compound under review can be measured if experimental conditions are comparable (see Appendix B).

If CAI's are to be useful for policy purposes, however, they must provide information on the dangers to humans of exposures to potential carcinogens such as certain pesticides. More precisely, the CAI's would have to allow for assertions and comparisons such as, "ingestion of *x* m moles of endrin has about the same probability of inducing a cancer as ingestion of 10*x* m moles of chloroform." A number of assumptions must be made before such assertions based on experimentally observed CAI's can be justified. One set of assumptions that permits useful inferences to be drawn about the effect of specific pesticides on human health is suggested and discussed in Appendix B. The reader is urged to read and consider those assumptions. One will see that they are not innocuous and that, though intuitively appealing, they have little experimental support. The reason for preferring the evaluation of risks by means of CAI's to the current procedures is that the current procedures require substantially stronger and less plausible assumptions and produce an end product that is much more liable to misinterpretation.

In spite of the limitations that have been noted, the Committee feels that potency indexes, such as the CAI's, are the best indicators available of the relative danger of different pesticides. Responsible officials and the general public should be informed of such indicators (together with the ranges of experimental error and uncertainty to which they are subject), and regulatory decisions should take them into account. The Committee recognizes that it would be more convenient if regulatory decisions could be based on reliable estimates of the probable effects of different regulatory options on human morbidity and mortality. But such estimates cannot be justified given the current state of scientific knowledge.

Accordingly:

- *The Committee recommends that when laboratory data are used to estimate pathological activity, potency indexes, such as the* CAI*'s defined above, be used to indicate the pathological virulence of the pesticide under consideration and that no numerical estimates of effects on human morbidity or mortality be extrapolated from laboratory data. The estimated potency indexes should be presented as most probable values accompanied by indications of ranges of uncertainty.*

How the CAI's can be taken into account will be discussed further below and again in Chapter 6, and illustrated in Chapter 7.

COMBINING EXPOSURE AND PATHOLOGICAL ACTIVITY

Estimates of exposure and pathological activity must be combined in appraising the hazard to human health posed by the use of a pesticide. The current procedure, to be discussed more fully below, is to make the combination by calculating, for each relevant segment of the population, an estimate of the probability that an individual will contract a disease (such as cancer) as a consequence of the use of the pesticide. The preceding discussion indicated that available estimates of the effects of pesticide use on incidence of disease in humans do not merit scientific credence. Therefore, the Committee recommends that the practice of making such estimates be abandoned. At the same time, the procedures for appraising pathological activity recommended by the Committee do not, in principle, lend themselves to similar, quantitative estimates of effects on human morbidity or mortality. Thus, different methods must be used to combine exposure and pathological information. The current methods and a recommended alternative are discussed in the following two subsections.

Current Practice

The risks incurred by the use of any pesticide vary. They include carcinogenicity, mutagenicity, other chronic health impairments, and acute reactions. There are also risks to natural biota and to agriculture and livestock. The overall assessment of risks must take all these possibilities into account. For this reason, and perhaps others, the risk assessments in available OPP position documents have not followed a standard format. The risks associated with a pesticide have been appraised by various methods, taking account of the nature of the predominant risks of concern as well as characteristics of the available data.

The appraisals share certain fundamental features, however. For example, as noted previously, the risks associated with cancer are estimated by the CAG primarily on the basis of animal bioassay data and evaluations of the metabolic and toxicological characteristics of the compound. Other hazards to human health are appraised by OPP's HED, using similar types of data and epidemiological evidence when available. Hazards to wildlife or biota and potential crop or livestock damage are evaluated by HED also, through searches of the relevant literature. The USDA/EPA benefit assessment teams play an important role in acquiring information about the use of pesticides that may generate such hazards. Potential and actual exposures are estimated, as described above, by well-standardized methods. In the end, these diverse kinds of information must be pulled together, and it is at this point that standardization ceases. Two examples will suffice.

In the appraisal of chlorobenzilate (U.S. EPA 1978a), the induction of cancers was judged to be the primary type of risk with which to be concerned. Accordingly, factors provided by CAG were used to infer the increase in the lifetime probability of contracting cancer that would result from the continued use of chlorobenzilate. Separate factors were computed for different segments of the population to allow for the different lifetime doses to which people would be exposed. For example, the general U.S. population is exposed to very low doses by eating foods on or in which residues of the chemical remain, while applicators receive much higher doses through dermal and inhalation exposure (see Chapter 7). The risk analysis data were therefore summarized by displaying the increase in the maximum, or worst-case, lifetime probability of contracting cancer for members of each of seven population groups and for seven possible regulatory options (see Table 6.1).

In the analysis of the risk associated with endrin (U.S. EPA 1978b), not cancer but the likelihood of teratogenesis was the primary concern. Three groups of women may be exposed to significant doses of endrin: female pilots of endrin-spraying aircraft (probably a very small number of women), downwind neighbors exposed during the spraying operation, and women who eat fish from water contaminated by runoff and drainage from fields treated by endrin. For each of these groups a plausible daily dose (in milligrams per kilogram) was estimated and a margin of safety was computed according to the formula:

$$\text{Margin of Safety} = \frac{\text{Largest dose for which no effects were observed in experimental animals}}{\text{Dose to which some (perhaps few) members of the population may be exposed}}.$$

A margin of safety of 300 or less was judged to indicate a significant risk.

In general, as suggested by these illustrations, there is no attempt to be uniform in assessing the potentials of different pesticides for harming public health, wildlife, materials, and crops. Each analysis is adapted to particular circumstances.

Comments and Recommendations

The practices described above, representing current attempts to quantify the risks of using different pesticides, suffer from at least two serious deficiencies. The first is the noncomparability of the risks estimated for one pesticide with those of another estimated in a different form. The second, which was discussed at length above, is the unreliability inherent in estimates of change in human morbidity or mortality extrapolated from experiments with animals.

The lack of comparability is a consequence of the wide variety of ways in which a pesticide may inflict harm. There is no defensible formula for reducing all varieties of damage to human health to a common index of seriousness. Nevertheless, it is important that when similar consequences are at issue, they be estimated and reported in comparable ways. If this can be done, serious inconsistencies among decisions relating to different compounds will be minimized and the accumulation of useful experience in appraising risks, on the part of both the Administrator and the staff, will be facilitated.

The appraisal of risks to human health can be systematized by applying the concept of the CAI together with analogous concepts. We have already discussed at length problems of measuring and expressing the potential carcinogenicity of a compound, and we concluded that the best method, generally, is to indicate carcinogenic activity relative to that of other compounds using a CAI. The indicator must then be combined with estimates of the numbers of people exposed to different doses of the compound to yield an overall assessment of the cancer risk that is posed. The question is how to do this.

It is not meaningful to combine the CAI with estimates of exposure by multiplying them or by any other simple arithmetic formula. Some people—like pesticide applicators—are exposed to doses several orders of magnitude greater than others are exposed to. In the absence of a dose-response curve applicable to humans, it is not possible to aggregate the different population segments receiving widely different doses into an overall estimate of the effect of the use of a pesticide on public health. In terms of effect on public health, 1,000 *N* people each receiving a dose of *D* is not equivalent to *N* people each receiving a dose of 1,000 *D*, nor do we know of any reliable way to compare the effects of the two exposures. The results must be presented as a table or graph that shows the numbers of people exposed to different doses. Furthermore, the dose to which each population segment is exposed may be different under different regulatory options, the effects of which can be indicated by a comparative exposure graph as illustrated in Figure 4.2. The illustration compares the doses to which three population segments are exposed under four regulatory options of increasing stringency. The CAI's must be used in preparing such a comparison.

To illustrate, let us suppose that Option A in Figure 4.2 is the unrestricted use of pesticide *X* while Option B involves banning its use in certain areas. The farmers in the prohibited areas can then be expected to resort to other expedients: some might use pesticide *Y*, others pesticide *Z*, others biological controls, and so on. The effect of these changes on exposure to pesticides *X*, *Y*, and *Z* cannot be foreseen with

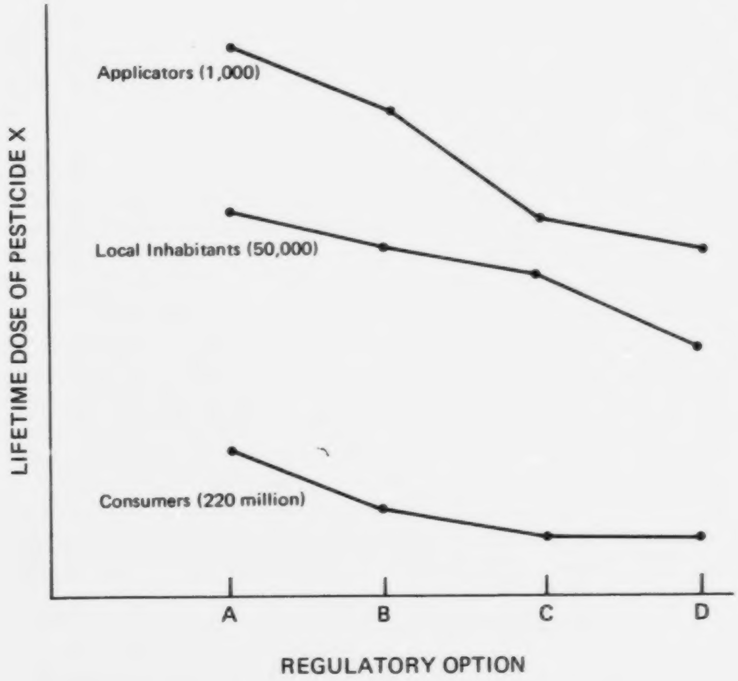

FIGURE 4.2 Comparative exposure graph (schematic).

precision, but it can be approximated with the help of the CAI's. Suppose, for example, that under Option B when pesticide *X* is banned, P_y percent of the crop will be treated with the substitute pesticide *Y*, P_z with pesticide *Z*, and so on. Using the assumptions described in Appendix B, it can be shown that if doses D_x and D_y are not very dissimilar, the applicator population, for example, is consequently exposed to pesticide *Y* at a dose equivalent to D_y^e units of pesticide *X* where

$$D_y^{\,e} = \frac{\mathrm{CAI}_y}{\mathrm{CAI}_x} D_y \, .$$

That is, D_y^e is the dose of pesticide *X* that produces the equivalent pathological effect of the dose of pesticide *Y* that applicators might be expected to receive under regulatory Option B. The same will pertain for pesticide Z. *In toto*, the average exposure of applicators under Option B in terms of pesticide X equivalents will be

$$P_xD_x + P_yD_y{}^e + P_zD_z{}^e \ldots .$$

This is the number to be plotted on the chart. The approximating assumption used in making the comparison is that pathological response is proportional to dose for moderate ranges of doses, though not for large variations. Where better approximations are known (e.g., linearity instead of proportionality), they should be used.

To this point, the risks associated with different options have been expressed in units of exposure to the pesticide under consideration. A final step in the presentation is to note, again using the CAI's, how the carcinogenic activity of the pesticide compares with the activities of other pesticides currently in use or previously regulated. These comparisons are discussed in Chapter 6, where benefits of the different regulatory options are compared with their risks, and later illustrated in Chapter 7.

Again, the Committee has not studied other risks to public health as carefully as it has studied carcinogenicity. Nevertheless, it believes that many of the problems of appraising risks of mutagenicity, teratogenicity, and acute and chronic toxicity in humans are closely analogous to those encountered in the analysis of cancer risks to the extent that reliance is placed on extrapolations from bioassays using laboratory animals. The same methods of risk assessment should therefore apply. Indicators must be constructed showing the comparative potencies of different compounds in inducing mutations, abnormal offspring, and toxic effects. Consequences of different regulatory options can then be compared by the methods just described, using the appropriate activity indicators and, when available, human data.

ANALYSIS OF ENVIRONMENTAL RISKS

In addition to considering the risks to human health posed by an RPAR compound, the Agency is also obligated under 40 CFR 162.11 to identify and weigh any environmental risks associated with the chemical. Specifically, the environmental risk triggers are (1) acute toxicity to nontarget species, (2) chronic toxicity to members of endangered species, and (3) chronic toxicity to nontarget species (see Note to Chapter 2).

The environmental risk analyses performed by OPP's HED are somewhat analogous to the human health risk analyses. In particular, the environmental risk analyses attempt to determine the extent to which current use and exposure patterns, and the use-exposure patterns likely to arise under the various regulatory options, may prove lethal to nontarget organisms.

OPP's environmental analyses are based upon either theoretical considerations or empirical evidence. For instance, OPP's presumption that endrin is acutely toxic to rabbits and pheasants was based on theoretical calculations of the endrin residues likely to be found on items consumed by these animals (U.S. EPA 1978b:13). The theoretical arguments were eventually modified to reflect the findings of actual residue studies submitted by an endrin registrant (U.S. EPA 1978b:14). In contrast to the acute toxicity presumption, the presumption that endrin is responsible for significant reductions in nontarget populations was based upon actual data on fish kills derived from the Pesticide Episode Reporting System (U.S. EPA 1978b:18).

Unfortunately, the data available on environmental hazards are often too incomplete to allow for the development of accurate, quantitative risk estimates. Realistically, there is currently no way of developing reliable estimates of, for example, the number of rabbits or pheasants that die each year from ingesting endrin residue on forage or seeds. Even in cases involving significant local population reductions, such as large fish kills, OPP may have little or no quantitative (or even qualitative) evidence. Position Document 2/3 for endrin notes, for example, that the Pesticide Episode Reporting System (which depends on voluntary reporting) is so unreliable that it missed at least 20 endrin-related fish kills over a 5-year period in Mississippi. As a result of these data shortages, the environmental risk analyses tend to rely heavily upon sketchy, perhaps even qualitative, information.

The Committee has focused its attention in this report on health effects. This is not to say that it felt the assessment of environmental risks is not significant, but only to confess that the Committee chose not to study it in depth itself. Nevertheless, it is clear to the Committee that an improved data base is necessary. To this end, and on the basis of the Committee's observations and review of selected OPP position documents, we suggest that EPA (1) devote more resources to environmental monitoring and (2) initiate more studies of environmental toxicology of selected pesticides. When quantitative environmental risk analyses are made, we further recommend that estimates be reported as ranges. As for human exposure analyses, the ranges should be presented as a pair of numbers, one showing the most-probable environmental risk and the other showing the maximum-plausible estimate.

RISKS TO STRUCTURES, MATERIALS, AND CROPS

Generally speaking, risks to structures and materials entailed by the use of pesticides are negligible. On the other hand, pesticides may be harmful to crops grown in nearby fields, to livestock, or to commercial fisheries. In the latter instances, current practice is to estimate the monetary value of the decreases in yield or increases in cost of maintenance estimated to result from use of the pesticide. In the Committee's judgment, the methods currently used for making these estimates are straightforward and sound, although we recommend that such estimates be derived and reported for both the most-probable and maximum-plausible cases.

OVERALL ASSESSMENT OF RISKS

The use of any pesticide entails a complex bundle of risks: risks to the health of different segments of the population, to wildlife, to vegetation, to crops and livestock, and to buildings and materials. Each of these risks is a result of several factors: the number of vulnerable elements exposed to the pesticide, the dose to which each element is exposed, and the potency or harmfulness of the pesticide.

At some stage in the evaluation of regulatory options, appraisals of the different kinds of risks must be combined and compared with the costs of different options. How to consolidate appraisals of the individual types of risks and the extent to which they can be consolidated are among the principal concerns of Chapter 6. The assessments of the several types of risk reviewed in this chapter are necessary ingredients in that final appraisal.

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5 Benefit Assessment

INTRODUCTION

If EPA determines that a pesticide meets or exceeds the risk criteria defined in 40 CFR 162.11 (see Chapters 2 and 4), the Agency is obligated to issue an RPAR. If the presumption of risk is not successfully rebutted, some type of regulatory response is likely to be forthcoming. In making a determination as to the specific form the response should take, the Agency is allowed by 40 CFR 162.11 to take into consideration the findings of an analysis of the benefits arising from the use of a pesticide. Moreover, analyses of the economic and social impacts of pesticide regulatory actions are required by the FEPCA of 1972 and its subsequent amendments. The purpose of this chapter is to examine critically the current USDA/EPA approach to assessing the benefits of pesticide usage and, where appropriate, to recommend certain changes in that approach.

This chapter argues that OPP's benefit-risk methodology could be improved by better use of standard analytical procedures. At the outset, we wish to make it clear that federal pesticide law does not require the use of a formal benefit-cost (or risk) analysis. Except where a statute expressly so provides, the courts have not interpreted a statutory duty to balance benefits against costs to require a formal benefit-cost (or risk) analysis. Instead, agencies like EPA have taken it upon themselves to adapt formal benefit-risk methodology to the regulatory problem at hand. The difference between a duty to carry out a formal benefit-risk analysis and to balance benefits against risks is significant, for the degree of rigor required by the latter is much less than that required by the former. If an agency undertakes a formal benefit-risk analysis, it should use the best available state of the art; we offer some suggestions for improving the procedures that OPP has voluntarily agreed to follow.

Before turning to a critical evaluation, two introductory and clarifying comments are in order. The first is definitional. In connection with the evaluation of government regulations, the term "benefit" is usually employed to describe the advantages of a regulation such as the improvement in human health that will result from prohibiting the use of a hazardous pesticide (see, for example, NRC 1977). Consequently, the reader is cautioned that USDA/EPA defines benefits differently. Specifically, "benefits" are defined as desirable effects resulting from continued use of a pesticide. In this context, a regulatory action limiting the use of a pesticide would result in a reduction in risks and a loss of benefits. This report adheres to the definitions employed by the USDA/EPA analysts.

The second point is concerned with the presumed objectives of a benefit assessment. In keeping with conventional principles of benefit-cost analysis (which are discussed in more detail later in this chapter), a benefit assessment should strive to meet two separate but related objectives. First, a benefit assessment should attempt to measure the "real" (or economic efficiency) benefits of a pesticide—that is, the extent to which use of a pesticide contributes to the available quantity of desirable goods and services, thereby enhancing society's standard of living. Second, a benefit assessment should attempt to identify and quantify the distributional effects (or "economic impacts") associated with use of a pesticide. In principle, a distributional (or economic impact) analysis involves more than a determination of how the real benefits are spread among various groups. It also encompasses an assessment of the distribution of "pecuniary" effects (that is, transfers of purchasing power from one group to another arising out of price changes). The distinction between economic efficiency effects and distributional impacts is important and will be emphasized in our discussion.

This chapter is devoted to procedures and methods for assessing the benefits of using particular pesticides; since most pesticides (almost 75 percent by volume, U.S. EPA 1979b) are used in the production of food and fiber, the discussion is framed primarily in terms of the agricultural uses of pesticides. This is not to say that the Committee believes nonagricultural uses do not pose significant human health and environmental risks. Rather, the Committee had to limit the scope of its review and chose agricultural uses since OPP devotes a majority of its effort to this area.

The discussion is divided into the following major parts. The first section considers the problems associated with measurement of pesticide productivity, that is, the extent to which use of a chemical increases production of things people value. The second section focuses on the problem of estimating how much the use of a specific pesticide reduces pest control costs and other production costs. These two components—pesticide productivity and cost savings—are brought together in the third section, which presents appropriate methods for measuring the real benefits of pesticide usage and for distributing both real and pecuniary effects among certain key groups.

Our critical evaluation of the methods currently employed by USDA/EPA economists to assess benefits of pesticide use is based upon a review of several actual benefit assessments, namely, those for chlorobenzilate (Luttner 1977a, b), DBCP (U.S. EPA/USDA 1978a), endrin (Luttner 1977c, Mattson *et al.* 1977), lindane (U.S. EPA/USDA 1978c), toxaphene (U.S. EPA/USDA 1978b), and trifluralin (USDA *et al.* 1977). These six assessments consist of fifty-eight separate use-pattern assessments or analyses, with each analysis focusing on a specific use of a pesticide. For instance, the trifluralin assessment consists of six separate analyses for uses on cotton, soybeans, other field crops, fruits and vegetables, miscellaneous crops, and noncrop sites.

ANALYSIS OF PESTICIDE PRODUCTIVITY

Pesticides are toxic chemicals used to kill a variety of organisms (e.g., rodents, insects, pathogens, and weeds) that people consider objectionable for any one of several reasons. Many organisms are viewed as pests because they interfere with agricultural and forestry production. Others transmit diseases to humans and thus pose a hazard to public health. Finally, some organisms, such as household lawn and garden pests, create nuisances or aesthetic problems. For whatever reason, control of pest organisms offers certain advantages, such as improvements in food and fiber yields and the quality of products or reductions in the incidence of human disease. A regulatory decision to prohibit or otherwise restrict the use of a pesticide may consequently force society to forgo substantial benefits.

A crucial first step in analyzing benefits offered by a pesticide is an assessment of that pesticide's productivity—that is, its effectiveness at providing something that people value, such as higher crop yields. Of course, if a pesticide has a detrimental impact on nontarget organisms resulting in negative productivity, such an impact must also be included in an assessment of the pesticide's effects.

Pesticide productivity is not the same as pesticide efficacy. "Efficacy" refers to the pesticide's effectiveness at reducing a pest population, whereas, in this context, "productivity" refers to the pesticide's effectiveness at providing more or better food and fiber, improvements in public health, or more attractive surroundings. Thus, a highly efficacious pesticide would be relatively unproductive if its target organism actually had little effect on, say, crop yield or quality. Pesticide efficacy and productivity are related but quite clearly different concepts. This part of the chapter focuses on the issue of pesticide productivity.

CURRENT APPROACH: METHODOLOGY AND DATA

The USDA/EPA procedure for evaluating the productivity of an agricultural pesticide concentrates on quantifying the pesticide's effects on crop yield or output. The possibility that quality effects may also be important is, of course, recognized in the USDA/EPA benefit assessments; however, data are generally inadequate to quantify such effects. Post-harvest losses resulting from pre-harvest infections by pests are also often omitted because of lack of data.

In estimating yield effects, an attempt is made to measure the change in output (e.g., bushels of corn reaching the marketplace) that would occur if a particular chemical were withdrawn from the market and replaced by alternative chemical or nonchemical methods of pest control. The estimation requires two basic types of data: (1) an indication of the extent to which each of the various alternatives would be employed as a substitute for the suspect chemical, and (2) an estimate of differences in yield or output between the suspect chemical and the alternatives. Unfortunately, these data are not always available. Consequently, the benefit assessments are sometimes forced to consider these important aspects of productivity in qualitative terms only. For instance, 18 of the 58 use-pattern assessments reviewed for this chapter contain no quantitative evaluation of the impacts of cancellation.

Primary responsibility for assembling evidence on the productivity of a pesticide and its alternatives falls to the USDA/EPA benefit assessment team (see Chapter 2). More specifically, the biologists (e.g., entomologists, plant pathologists) on the assessment team are responsible for providing estimates of yield and, if possible, quality effects. Often these data are developed from published sources, but the team biologists may also rely upon their own judgment or upon other unpublished sources such as personal communications with other pest control specialists.

RECOMMENDED APPROACH

The measures of pesticide productivity that the USDA/EPA benefit assessments attempt to implement are basically sound; that is, the assessments define pesticide productivity correctly. Of course, it does not follow that the actual estimates of pesticide productivity will be accurate. As is noted at various points in this chapter, incomplete data often prevent the analyst from making more than a very crude estimate of the productivity of a pesticide. There are some problems with the current method of predicting the use pattern that would arise among the alternatives were a suspect chemical to be withdrawn; however, discussion of the problems are deferred until later in this chapter.

Another methodological problem arises not only in connection with estimating pesticide productivity, but also throughout most of the benefit analyses. Specifically, USDA/EPA estimates of yields (and of other benefits) are usually expressed as clearly determined magnitudes even though there may be considerable uncertainty about their accuracy. The practice lends an unjustifiable aura of precision to the benefit estimates. In general, an uncertain measure should be reported as an interval—a probable estimate with upper- and lower-bound estimates—rather than as a single number.

The central recommendation specific to the measurement of pesticide productivity relates to the current procedure for assembling the yield and quality data. Benefit assessments currently place excessive reliance on "data," often unpublished, and sometimes contained in controversial reports, that have not been subjected to conventional scientific tests of validity.

The credibility of a benefit analysis depends ultimately upon the credibility of the data that support it. Of course, the regulatory process cannot await the generation of a complete set of sound scientific data. However, the regulatory process can, and should, demand that benefit (and risk) analyses be performed with the best available data and with data that have withstood some scrutiny.

The problem with the current procedure for assembling benefit data is illustrated by the USDA/EPA analyses for the pesticides chlorobenzilate and dimethoate. Data for these analyses were obtained mainly from unpublished reports and personal communications with pesticide specialists. A few relevant published studies were identified by OPP with the aid of several computerized bibliographic indexes. However, literature searches commissioned by this Committee identified numerous important published studies that were either missed or intentionally omitted by the USDA/EPA procedure (see Chapter 7 and Appendix D). Moreover, the independent literature searches revealed that the data obtained through personal communications on balance differed significantly from the published information. For several pests and crops, the chlorobenzilate and dimethoate data derived from unpublished sources tended to overstate the benefits of the suspect chemical.

The recommended procedure for assembling an acceptable data base for a benefit analysis involves the following steps. First, a thorough search of the published literature must be undertaken. The literature search should use all major indexing bibliographies, and recent issues of relevant, but unindexed, scientific journals should also be examined. Computerized indexing services may be of some supplemental use in this literature search, but they are too far from being complete to be relied upon as the sole guide to relevant literature.

Whenever feasible, data on use of the suspect chemical and its alternatives outside the United States should also be assembled. Although it may not be appropriate to use such data directly, they may provide helpful support to the data based on U.S. experience.

After the published literature has been searched thoroughly, it might prove useful to consult some unpublished sources in the form of unpublished reports or perhaps the firsthand knowledge of pest control specialists. Each specialist contacted should be informed of the relevant published information concerning the pest or pesticide and encouraged to think in terms of a *total accounting* of all major losses of the commodity in question due to pests. Presumably, the broader perspective will help reduce the likelihood that the yield or quality effects attributed to any one pesticide or to any one pest will be either exaggerated or understated. The problem of overestimating yield effects is especially troublesome. The pest control literature offers examples in which estimates of aggregate yield losses from the combined effect of insects and other pests exceed 100 percent (Pimentel *et al.* 1978).

Once data on productivity effects of both chemical and nonchemical alternatives have been assembled, such data should be further validated for thoroughness and accuracy through critical internal and external reviews by knowledgeable scientists. At present, it is the legal responsibility of the SAP to provide an external scientific review of OPP's health and environmental hazard assessments. In practice, the SAP has also provided some review of the benefits analysis (see SAP comments published with EPA's notice of final determination on chlorobenzilate, U.S. EPA 1979a), but the arrangement results in inadequate reviews of the benefits data and analyses. Since the involvement of the SAP is limited largely to the final stages of the RPAR process (see Chapter 2), the SAP is confronted with the task of reviewing analyses that are virtually complete and thus unlikely to be changed in any significant way. The usefulness of such reviews could be enhanced greatly through earlier SAP involvement in the analyses. An additional problem with the current scientific review procedure is that the SAP was created, and its membership chosen, primarily to provide a review of risk-related issues. Consequently, benefits data and analyses appear to receive relatively little attention from individuals chosen for their expertise in the benefits area.

For these reasons, the Committee makes the following recommendation:

- OPP *should establish an external Benefits Review Panel, similar in organization to the* SAP, *consisting of entomologists, plant pathologists, weed specialists, economists, and others with expertise in the assessment of benefits. The panel would have the responsibility of providing external scientific reviews of the benefits data and analyses. For each* RPAR *compound, a review team (consisting for example of one entomologist and one economist) should be selected from the panel. This team, in contrast to current* SAP *procedures, should be involved from the earliest stages of the benefits assessment, and should have primary responsibility for presenting an evaluation of the assessment to the entire Benefits Review Panel.*

ESTIMATING CHANGES IN PEST CONTROL COSTS

CURRENT APPROACH

The second key component of a benefit analysis is an assessment of the effect that withdrawal of an RPAR chemical would have on pest control costs. (Other costs of cultivation or production may also be important and are considered later in this chapter.) The operational definition that OPP attempts to implement for each specific use of the suspect chemical is (assuming the treated item is a crop):

$$\Delta PC_i = \sum_{j=1}^{J} \Delta\,[A_j T_j\,(MC_j + AC_j)] \;-\; \sum_{k=1}^{K} \Delta\,[A_k T_k (MC_k + AC_k)],$$

where ΔPC_i is the change in pest control costs for the ith use of the RPAR chemical (e.g., a particular crop in a certain region); j denotes one of the J pest control methods not involving the suspect chemical; k indicates one of the K control methods employing the suspect chemical; A_j and A_k are the number of acres treated per year by methods j and k, respectively (sometimes referred to as "base acres"); T_j and T_k are the average number of treatments per year by methods j and k, respectively; MC_j and MC_k are material costs per acre-treatment; and AC_j and AC_k are application or treatment costs per acre-treatment.

The data for implementing this measure come from a variety of sources. Much of the information (e.g., the number of acres treated) is supposed to be developed by the USDA/EPA benefit assessment team. Although it is difficult to generalize about the data sources employed by the assessment teams, there appears to be fairly extensive reliance upon unpublished sources and the judgments of individual team members or other specialists. In certain instances some of the data are obtained from surveys, especially those provided by Doane Agricultural Service, Inc. Finally, some of the data used are simply plausible assumptions. For instance, benefit analyses commonly suppose that the number of acres treated would not be affected by withdrawal of the RPAR chemical (e.g., see Luttner 1977a).

RECOMMENDED APPROACH

For the most part, the current approach to estimating the change in pest control costs is sound, but there are some aspects that should be altered.

First, the imprecision of many of the estimates is obscured by the practice of reporting point estimates rather than interval estimates. As a general rule, OPP's benefit assessments should be more forthright about the uncertainty surrounding the estimates by reporting *plausible minimum and maximum values along with the most-probable estimates* for key variables.

A second recommendation relates to the current practice of estimating material and application costs with data obtained from a variety of sources. For example, OPP's chlorobenzilate benefit assessment (Luttner 1977a, b) employs information from the Doane Speciality Crops Survey, dealer price lists, and pest control specialists (especially those serving on the assessment team). Estimation of changes in pest control costs requires information about *differences* in material and application costs. Whenever feasible, these cost differentials should be estimated from a single, consistent set of data (e.g., dealer price lists) rather than from data generated from several sources. Estimating cost differentials with data obtained from several different sources or in a variety of ways inevitably heightens the inaccuracy associated with the estimates.

A third recommendation pertains to the current method of predicting the extent to which the various alternatives would actually substitute for a withdrawn RPAR chemical. In some instances the use-pattern forecast for the alternatives is based on unrealistic assumptions. For instance, the chlorobenzilate analysis assumes that the base acres treated with chlorobenzilate would be evenly divided among the several alternatives, even though there are significant cost differences among those alternatives. A benefit assessment should estimate changes in pest control cost using a more plausible assumption.

In the absence of information to the contrary, it would be reasonable to adopt, as a working hypothesis, the assumption that the relative distribution of base acres among alternatives is unaffected by withdrawal of the RPAR chemical (unless, of course, some of the alternatives were also likely to be withdrawn or otherwise restricted. As is noted in Chapter 3, in making these comparisons it is necessary to have a well-founded judgment as to which alternatives are likely to be permitted or cancelled.) That is, the increase in base acres treated with the *j*th alternative (ΔA_j) following cancellation of a suspect pesticide should be presumed to equal

$$\Delta A_j = p_j A_k ,$$

where A_k is total base acres treated with the RPAR chemical, and p_j is the ratio of (1) base acres currently treated with the *j*th alternative to (2) base acres currently treated with all of the alternatives to the RPAR pesticide. Even this estimation procedure is highly arbitrary and, whenever possible, should be amended to reflect the best available information.

ECONOMIC EVALUATION OF PRODUCTIVITY AND COST EFFECTS

This section appraises current USDA/EPA procedures for evaluating the productivity and cost effects of proposed pesticide regulations. Two related tasks are involved. The first is to assign values, generally monetary, to the real benefits (i.e., goods and services) that would be forgone were the compound to be withdrawn or its use otherwise restricted. The second task is to determine, to the extent feasible, the distribution of the benefits (which may be negative in some cases) among affected segments of the population. This section outlines the current USDA/EPA approach to these two tasks, compares it with standard methods of benefit-cost analysis, and recommends some changes in the USDA/EPA procedures. As noted at the outset of this chapter, the discussion is framed primarily in terms of agricultural uses of the suspect chemicals.

CURRENT APPROACH

The USDA/EPA benefit analyses all adopt a partial equilibrium framework referred to as "partial budgeting." In measuring the benefits that would be forgone if a pesticide's uses were restricted or cancelled, the USDA/EPA economists usually assume that proposed restrictions would significantly affect only (1) the quantity of substitute pesticides that would be used in place of the one that is restricted, and (2) the output of the treated item. Of course, for agricultural uses and most nonagricultural uses, changes in these two variables imply changes in production costs and revenues. In a few instances, the effects these changes would have on output prices is also taken into account (see, for instance, USDA *et al.* 1977). (The quantitative assessments of public health uses of pesticides assume that tighter restrictions on use of a suspect compound will significantly influence only the quantities of alternative pesticides applied in these uses [A.L. Aspelin, OPP, EPA, Washington, D.C., personal communication, October 1978].) Typically, other variables in the quantitative analyses are assumed to remain constant, including the quantity of other inputs to the productive process, input prices, and output quality. The benefit assessments usually note that these variables may change as the result of a regulatory action, but inadequacy of available data commonly prevents the analysts from developing quantitative estimates of these changes. In a few instances, estimates of output price changes are employed in evaluating the *distributional* (but not the economic efficiency) consequences of a regulatory action (see, for instance, Luttner 1977c and U.S. EPA/USDA 1978a).

The operational benefit measure currently used in the USDA/EPA assessments is the saving in pest control costs arising from continued use of the RPAR pesticide plus the value of the output that would be lost without the RPAR chemical. This concept can be expressed in equation form as:

$$\text{USDA/EPA annual benefit measure} = (PC_s - PC_r) + (P_r X_r - P_r X'_s), \qquad (5.1)$$

where PC_s is equal to the aggregate annual pest control costs with only the substitute controls; PC_s is equal to the aggregate annual pest control costs with the RPAR chemical; P_r is the price per unit of output (e.g., of a crop), assumed constant (estimated, for example, by the average of the previous 3 years); X_r is the annual output (e.g., total crop produced) if the RPAR pesticide is available; and X'_s is the annual output that would be produced in the absence of the suspect chemical, assuming the price P_r remains constant. Of the 58 use-pattern assessments reviewed, 21 estimate both components of the above benefit definition. Another 19 of the assessments estimate only the expected change in pest control costs ($PC_s - PC_r$); they assume that the substitutes are as efficacious as the RPAR chemical. This assumption is often adopted because data on actual yield differences are unavailable. The remaining 18 assessments contain no quantitative evaluation of the economic impacts of a cancellation. It is often necessary to rely upon qualitative assessments because data are either nonexistent or inaccessible, or time and resources are inadequate to undertake quantitative analyses.

In some instances the benefit assessments intermix estimates of the *real* benefits of a compound with estimates of the *monetary* gains and losses associated with use of the compound (see, for example, USDA *et al.* 1977). This practice of combining estimates of real and pecuniary effects will sometimes obscure the underlying definitions and methods used by the USDA/EPA analysts in measuring the separate effects. We will return to this issue in a later part of this chapter.

Treatment of Uncertainty

The basic USDA/EPA approach to coping with uncertainty about the magnitudes of key variables in the quantitative benefit assessment is simply to omit highly uncertain variables. For instance, of the 40 quantitative use-pattern assessments reviewed (an additional 18 were nonquantitative), 19 assumed that cancellation would not reduce the yields of the crop in question. The assumption was adopted primarily because of lack of data concerning the comparative effects on yields of different pest control measures.

The USDA/EPA benefit assessments treat the uncertainties of long-run effects in the same spirit. The assessments generally adopt a short-run perspective (3–5 years) to avoid uncertainties inherent in long-run forecasts of such key factors as technological changes in pest control or development of pest resistance to a compound (H. Gaede, OPP, EPA, Washington, D.C., personal communication, October 1978).

Some of the assessments use "sensitivity analysis" to generate alternative estimates for certain variables. Apparently this procedure is used only when there is some conflict in, say, estimates of yield effects reported in different studies. Sensitivity analysis is not routinely used to estimate *upper-* and *lower-*bound values, that is, to convert the analyst's (or an "expert's") judgment about best and worst possible outcomes (e.g., yield losses) into upper- and lower-bound estimates of the overall economic impact of a regulatory action.

Finally, the *expected value* approach to dealing with uncertainty about the magnitudes of key variables is employed in a number of instances. For instance, in the endrin/small-grains assessment, information about the historical frequency of "high" and "low" pest infestations and the accompanying yield losses in the absence of endrin are combined in the computation of an expected yield loss. In addition, estimates of pesticide prices are often based upon expected value calculations. Usually, however, too little is known about a variable's distribution to support formal expected value calculations (unless they are based on subjective judgments about the distribution).

Discounting

Only six of the assessments reviewed discounted future values to convert them to present-value equivalents. (The assessments used—without explicit justification—a 7 percent discount rate.) The practice of stating estimated effects in annual terms, combined with the short-run perspective, provides the USDA/EPA rationale for not discounting future effects in the majority of assessments. In general, discounting seems to be used only when output effects following a regulatory action are partially delayed for some years, as, for example, in the case of lengthy harvest cycles.

Distribution of Gains and Losses

Once the various economic effects of a proposed pesticide regulation are quantified, there remains the problem of determining how those effects are distributed across population and economic groups. For the most part, the quantitative USDA/EPA assessments assume that the burden of a regulatory decision will be borne largely by the users of the RPAR pesticide. The impacts of a regulatory decision on consumers or nonusers of the RPAR pesticide are usually discussed in qualitative terms, although in a few instances, such as the DBCP citrus assessment, the effects of alternative regulations on consumers and nonusers are analyzed quantitatively.

RECOMMENDED APPROACH

In this section the USDA/EPA approach to benefit assessment (described above) is compared with standard methods of benefit-cost analysis. (For textbook treatments of the general principles of benefit-cost analysis, see, for example, Anderson and Settle 1977, Mishan 1976, and Sugden and Williams 1978; for an application involving pesticides, see Headley and Lewis 1967 and Kennedy *et al.* 1975.) The discussion concentrates on those aspects of the current methods used by USDA/EPA that appear inconsistent with accepted principles of benefit-cost analysis. Some of these inconsistencies may be justifiable because of data problems, time constraints, and budgetary limitations. Others seem less defensible, however, and it is these shortcomings to which the Committee's recommendations are directed. It should be understood that the following discussion of conventional benefit-cost principles will not recommend that USDA/EPA discard their current approach in favor of the full-fledged ideal methodology. Rather, the purpose of developing benefit-cost principles is to provide a means for determining which feasible changes in the current USDA/EPA approach would actually represent improvements.

Economic Theory of the Benefits of Pesticide Use

Within the context of conventional benefit-cost analysis, the annual benefit of continued use of an RPAR chemical can be defined as the sum of (1) the value of productive resources saved due to use of the pesticide and (2) the value of any additional output arising from use of the RPAR chemical.[1] This definition does not allow for the cost of transferring resources among competing uses and for the capital losses from resources that cannot be transferred effectively. When these factors are important, allowance must be made for them or the benefits will be understated.

The value of productive resources saved can be expressed as:

$$TC_s - TC_r,$$

where TC_s is the total economic cost of producing X_s, the output that would be produced in the absence of the suspect chemical; and TC_r is the total economic cost of producing X_r, the output forthcoming with continued usage of the RPAR pesticide.

The relation involves *total* production costs, not simply pest control costs. Moreover, it allows for the possibility that output of the treated commodity will decline if use of the RPAR compound is restricted. It cannot be determined, *a priori*, whether TC_s is larger or smaller than TC_r, since output is allowed to vary. The RPAR chemical may well lower unit production costs; however, it may also cause *total* production costs to rise because of the additional production it stimulates.

To facilitate the following discussion, it will be useful to draw a distinction—an arbitrary one, but one implicitly made by USDA/EPA — between pest control costs (*PC*) and "other" production costs (denoted *OC*). Generally, the preliminary benefit analyses include as pest control costs only expenditures on pesticides and their application (see the preceding sections of this chapter). Of course, if nonchemical controls such as cultivation practices are feasible, it may be difficult to determine whether certain expenditures constitute pest control costs or "other" production costs. These considerations imply that

$$TC = PC + OC ;$$

consequently,

$$TC_s - TC_r = (PC_s - PC_r) + (OC_s - OC_r).$$

That is, the value of productive resources saved (if any) can be expressed as the change in pest control costs plus the change in other production costs.

The conventional measure for the value of increased output associated with use of an RPAR pesticide is the total willingness to pay for that additional output. Total willingness to pay for extra output consists of the sum of (1) the actual payments demanders would make ($P_r X_r - P_r X_s$); and (2) the consumers' surplus associated with that incremental output [$1/2(P_s - P_r)(X_r - X_s)$] (where the price and quantity that reign when the RPAR pesticide is available are indicated by P_r and X_r, respectively, and those that reign in the absence of that compound are denoted by P_s and X_s, respectively). The formulation assumes no externalities from the consumption of the agricultural commodity and, for convenience, a linear demand curve for the treated output. Even if the demand curve is nonlinear, the consumers' surplus measure (which reflects the availability of substitutes) will generally provide a reasonable approximation to the actual change in consumers' surplus.

Combining the two components of the conventional annual benefit measure,[2] we have:

Conventional annual benefit measure =

$$(TC_s - TC_r) + (P_r X_r - P_r X_s) + 1/2(P_s - P_r)(X_r - X_s). \qquad (5.2)$$

One further point to note in connection with the conventional benefit measure is that it includes a term for enforcement costs that would be avoided if the suspect chemical were simply (re)registered. In the preceding discussion we have neglected these costs, as do the USDA/EPA benefit analyses. In principle, such costs would have to be taken into account for the benefit measure to be fully consistent with conventional benefit-cost measures of economic efficiency effects.

Evaluation

A comparison of Equations 5.1 (the USDA/EPA annual benefit measure) and 5.2 (the conventional annual benefit measure) reveals a number of conceptual flaws in the USDA/EPA benefit measure. First, their measure omits the consumers' surplus component of Equation 5.2: $1/2(P_s - P_r)(X_r - X_s)$. The omission, which arises because they generally assume that output prices remain unaffected by a regulatory decision, would lead to an understatement of true benefits. To approximate this component of the correct benefit measure, one would need estimates of the price elasticities of demand and supply for the commodity in question.

The problem can be illustrated graphically with the aid of Figure 5.1, which depicts the competitive demand and supply conditions for a commodity both before and after cancellation of an RPAR pesticide. The pre- and post-cancellation equilibrium combinations of market price and output are (P_r, X_r) and (P_s, X_s), respectively. The consumers' surplus on the increment of output, $X_r - X_s$, equals area D in Figure 5.1. Graphically, it is this area that the USDA/EPA benefit measure omits.

It should be noted, however, that the omission of this component of consumers' surplus generally produces a minor understatement of true benefits. The chlorobenzilate analysis in Chapter 7 illustrates the point. The removal of chlorobenzilate is estimated to increase the costs of producing Florida oranges for processing by roughly $7.2 million annually. The maximum-plausible consumers' surplus loss in this instance is about $200,000. Consequently, failure to incorporate the $200,000 consumers' surplus component into the measure of benefits would understate true benefits by only about 2.8 percent. Moreover,

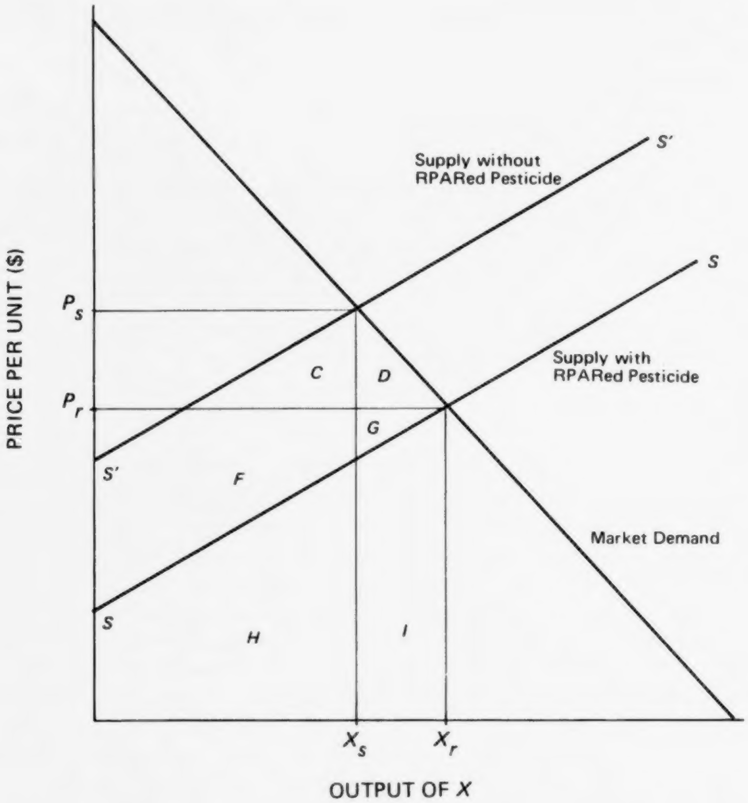

FIGURE 5.1 Competitive demand and supply conditions for commodity *X* before and after cancellation of an RPAR pesticide (see text for discussion).

omitting this small component from the benefit measure is probably justifiable in most instances, since the data are usually too crude to support such a refinement in the estimates.

Returning to the comparison of Equations 5.1 and 5.2, we note that the USDA/EPA operational benefit measure proxies the change in total production costs, $TC_s - TC_r$, with an estimate of the change in total pesticide treatment costs, $PC_s - PC_r$. The approximation to the actual change in total production may be defensible on the grounds that the change in total pesticide treatment costs can be estimated more easily than the change in total production costs. Generally, the available data simply do not permit estimation of changes in "other" production costs. Nevertheless, it should be noted that the procedure ignores any changes in "other" production costs, $OC_s - OC_r$, even though they will probably change if output changes or if failure to reregister induces changes in the methods of cultivation.

The role played by "other" production costs can also be illustrated in Figure 5.1. Again, the supply curves SS and $S'S'$ represent the competitive supply conditions with and without the suspect chemical, respectively. For purposes of this specific illustration, we adopt the simplifying assumption that $PC_s = PC_r$; that is, cancellation of the RPAR pesticide is assumed to have no effect on total (and, presumably, marginal) pest control costs. The assumption allows us to focus on changes in other production costs.

When the RPAR pesticide is used, total production costs are measured in Figure 5.1 by area $H + I$. In this example, cancellation of the chemical presumably reduces yield (unless the alternatives are equally efficacious), thereby shifting the supply curve to $S'S'$ where total production costs are $C + F + H$. Since pest control costs are assumed to be constant in this example, the change in total production costs is identical to the change in "other" production costs ($OC_s - OC_r$). Thus, $OC_s - OC_r$ is equal to $F + C - I$ in Figure 5.1. Depending upon market demand and supply elasticities, the change in "other" production costs can be either positive or negative.

Moreover, the USDA/EPA approach to estimating the change in pest control costs following a regulatory action ($PC_s - PC_r$) contains a number of conceptual problems. First, the usual USDA/EPA practice of assuming the quantities of nonpesticide inputs to be unaffected by the regulatory decision suggests that their estimate of PC_s may exceed its true value. Such an overstatement would occur, for example, if it were relatively cheaper, following cancellation of an RPAR pesticide, to simply plant more acres to offset yield losses than to employ substitute chemicals. The convenient assumption that nonpesticide input quantities remain constant rules out the realistic possibility that such inputs can serve as substitutes for pesticides.

Another conceptual problem with the USDA/EPA proxy for $PC_s - PC_r$, the change in pest control costs resulting from a regulatory action, also arises from the commonplace assumption that the number of acres treated remains unaffected by the regulatory decision. In fact, if the regulatory action occasions higher per-unit production costs and, ultimately, higher output prices, quantity demanded will decline (other things being equal), thereby possibly leading to a reduction in the number of acres treated with the substitute pesticides. If the acreage treated declines, the USDA/EPA estimates of the change in pest control costs will tend to be biased upward.

In summary, the USDA/EPA omission of the change in "other" production costs ($OC_s - OC_r$) from the benefit measure introduces a potential bias whose direction depends upon supply and demand elasticities. At the same time, their approach to measuring changes in pest control costs ($PC_s - PC_r$) has the potential of overstating the true value for this effect and, with it, the true value of the benefits from the RPAR chemical.

Another potential difficulty with the USDA/EPA operational benefit measure is that their estimates of $P_r X_r - P_s X_s$, a major component of willingness to pay for the additional yield allowed by the suspect pesticide, also tend to be biased upward. The reason lies in the usual USDA/EPA assumption that yield changes do not affect output prices. The point is illustrated in Figure 5.2, which again depicts the competitive demand and supply conditions for a commodity both before and after cancellation of the RPAR pesticide. The initial equilibrium price and output (with the RPAR pesticide) occurs at (P_r, X_r); the equilibrium following cancellation occurs at (P_s, X_s). Since OPP assumes that yield losses will not affect output prices, their estimator of the actual payment that demanders will make for the incremental output ($P_r X_r - P_r X_s$) is $P_r X_r - P_r X'_s$, or area $F' + G + H' + I$ in Figure 5.2. Clearly, this estimator will always overstate the true value of $P_r X_r - P_r X_s$, which is $G + I$ in Figure 5.2.

All of the various estimation problems can be summarized with reference to Equation 5.2 (rewritten as Equation 5.3 for convenience),

Conventional annual benefit measure

$$= (OC_s - OC_r) + (PC_s - PC_r) + (P_r X_r - P_r X_s) + 1/2(P_s - P_r)(X_r - X_s). \qquad (5.3)$$

The benefit methodology employed by OPP generally omits consideration of the change in "other" production costs ($OC_s - OC_r$) and of the consumers' surplus gain [$1/2(P_s - P_r)(X_r - X_s)$]. Omission of the consumers' surplus gain introduces a downward bias into the benefit estimate, although the magnitude of this bias is generally not very large. Omission of the change in "other" production costs has an uncertain effect on the accuracy of the benefit estimation. With regard to the change in pest treatment costs ($PC_s - PC_r$) and the amount demanders

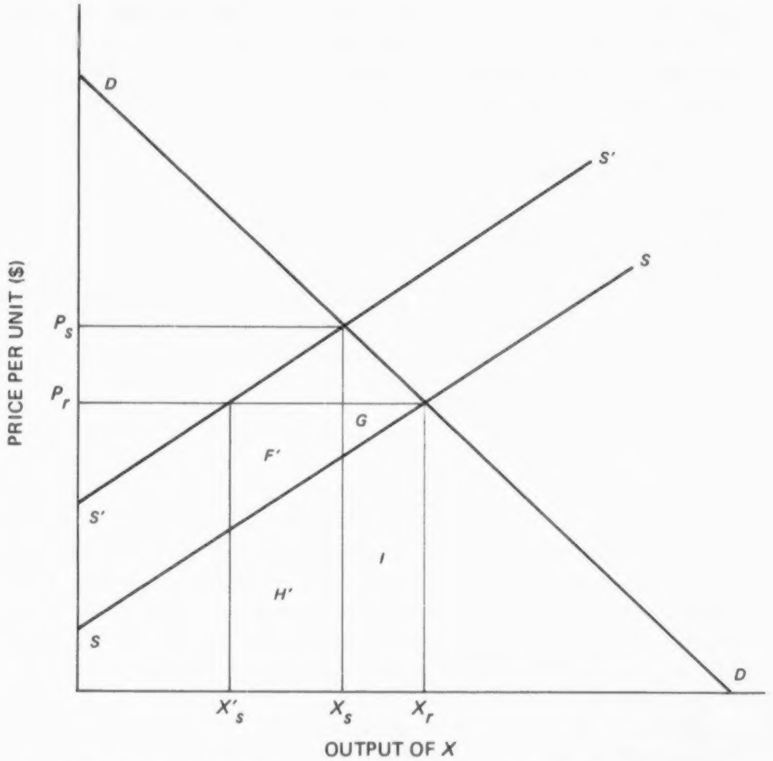

FIGURE 5.2 A bias in the USDA/EPA benefit measure (see text for discussion).

actually pay for the incremental output ($P_r X_r - P_r X_s$), the USDA/EPA approach tends to overstate both of these benefit components. On balance, the combination of biases working in different directions and the uncertainty about the bias associated with ($OC_s - OC_r$) imply that the EPA/USDA benefit estimator has the potential for either understating or overstating the true benefits of the RPAR pesticide.

Unfortunately, the quality of the data is generally so poor that there is little the USDA/EPA analysts can do at present about these potential biases. The kind of data currently available do not justify any more refined or elaborate methods for assessing benefits. Nevertheless, these sources of potential biases should be noted clearly in each benefit assessment. Needless to say, if the quality of the data improves over time, the potential sources of inaccuracies should be reduced or eliminated by altering the partial budgeting methdology so that it conforms more closely to the conventional methodology of benefit-cost analysis.

Treatment of Uncertainty

The only important change recommended in the USDA/EPA approach to dealing with uncertainty is to recognize openly the uncertainties surrounding the estimates presented and to indicate ranges of values, surrounding the most-probable estimate, within which the analysts feel some confidence that the true values lie. An ideal to strive for is the 90 percent confidence interval, even though such statistical precision will rarely be attainable.

Discounting

The USDA/EPA position on discounting is inconsistent in that some of the assessments (e.g., chlorobenzilate) discount while others avoid it. The function of discounting is to give costs or benefits to be received in the future a value comparable with costs incurred or benefits received in the present. The discounting procedure recognizes that people prefer returns sooner rather than later, that they prefer to postpone costs, and that all resources have alternative social uses or opportunity costs.

In the case of a chemical pesticide registration that is presumed against, the present value of the benefits or costs of cancelling that registration could differ significantly when discounted at a rate of interest of, for example, 8 percent from the present value rather than at an interest rate of zero. This would be especially true if the expected remaining life of the chemical in question were, for example, more than 4 or 5 years. The present value of a dollar to be received 5 years hence is $0.68 when discounted using an 8 percent interest rate. At the same rate of interest, a dollar to be received 9 years hence has a present value of only $0.50.

If a regulated chemical has an expected remaining life of 5–10 years, discounting the estimated stream of benefits from its continued use would provide a more accurate estimate of the social costs of restricting its use. However, before recommending that OPP adopt discounting for all benefit analyses, two important parameters need to be determined: (1) the length of time over which to apply discounting, and (2) the appropriate rate of interest.

The remaining useful or economic life of a chemical pesticide that is in use and subjected to RPAR action is likely to be in the range of 5–10 years (see Chapter 4, the section on Exposure Analysis). The economic termination of the use of a pesticide may be due to a loss in absolute or relative efficacy or both. Therefore OPP, after reviewing the literature on a compound, can determine a defensible useful lifespan. In Chapter 4, the Committee made a rough estimate that the economic lives of pesticides has averaged about 10 years.

Selection of an interest rate for discounting is the second important decision. Ideally, the rate chosen should reflect the real value that society places on future financial benefits and costs resulting from pesticide use. In past analyses (e.g., chlorobenzilate), OPP has used 7 percent as the interest rate for discounting. The Committee believes that this is a reasonable estimate of the real rate of return on investment in the economy after adjusting for inflation.

If the streams of benefits and costs of pesticide regulations are discounted in the fashion described above, the result should be a present value of net benefits for the remaining expected useful life of regulated compounds subjected to RPAR. This measure would help to differentiate between the value of compounds with similar annual benefits, but with different expected useful lives.

Distribution of Gains and Losses

The USDA/EPA benefit assessments are directed more toward measuring the *distributive* effects of a regulatory action (especially as the effects relate to the pesticide users) than toward quantifying the *economic efficiency* effects (A.L. Aspelin, OPP, EPA, Washington, D.C., personal communication, November 1978). Thus, it is important to compare the USDA/EPA approach to estimating the distributive effects with the methodology of conventional partial-equilibrium incidence analysis.

The conventional approach is illustrated in Figure 5.3, which represents the same short-run competitive supply and demand conditions as the preceding figures in this chapter. With the RPAR chemical available, total revenue from sale of the treated crop equals $P_r X_r$, or area $E + F + G + H + I$ in Figure 5.3. Initial short-run production costs (including a normal profit to growers) are measured by area $H + I$. Thus the initial economic profit or producers' surplus accruing to growers equals $E + F + G$. The total willingness of consumers to pay for output X_r is the entire area under the demand curve up to X_r, namely, $A + B + \ldots + H + I$. Since consumers actually pay $E + F + G + H + I$ for quantity X_r,

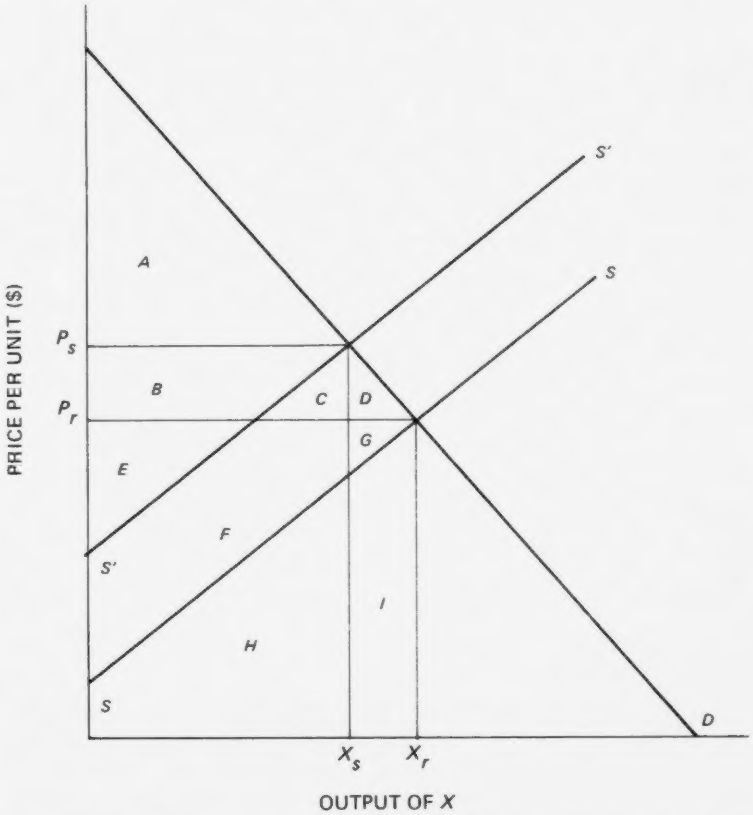

FIGURE 5.3 Distributional consequences of cancelling the registration of an RPAR pesticide (see text for discussion).

their initial net benefit or consumers' surplus from having X_r available at price P_r is equal to $A + B + C + D$.

Suppose that a regulatory action against the RPAR pesticide raises production costs and results eventually in a new equilibrium price and quantity of P_s and X_s, respectively. Total revenue is now $B + C + E + F + H$; total cost is $C + F + H$; producers' surplus is $B + E$; and consumers' surplus is area A.

The regulatory action has made consumers of X worse off by the amount $B + C + D$. Growers, however, may have been made either better off or worse off, since the *change* in producers' surplus equals $B - F - G$. Whether this change represents a gain or a loss depends upon the elasticities of the market supply and demand curves. We might also note that total revenue and total cost might either increase or decrease, depending on the shapes of the demand and cost curves: total industry revenue changes by $B + C - G - I$, whereas total industry cost changes by $F + C - I$.

Suppose that only a fraction of the growers of crop X use the RPAR pesticide. Under these circumstances, conventional incidence analysis suggests that if the regulatory action against the suspect chemical results in cost increases or output losses substantial enough to occasion price increases, then (1) consumers will clearly suffer, (2) nonusing growers will clearly benefit, and (3) users may suffer either gains or losses, depending upon demand and supply elasticities.

If the users of the RPAR pesticide are few relative to the total market, the regulatory action is unlikely to affect output prices. In this case, only the users suffer losses, which would be measured by their forgone economic profits (rather than revenue reductions). In general, the smaller the number of users relative to nonusers, the greater the likelihood that the entire burden of the regulatory action will be borne by the users.

A technical qualification to the preceding discussion is in order. The conventional approach assumes that reductions in the demand for productive inputs result in a virtually instantaneous transfer of those inputs into other equally productive activities. In reality, there will generally be some transitional unemployment as resources move from one productive activity to another. Incorporation of this effect into the conventional analysis would result in an increase in the costs of a regulatory action. Unfortunately the data available to the USDA/EPA analysts are generally inadequate for considering these transitional unemployment effects (H. Gaede, OPP, EPA, Washington, D.C., personal communication, October 1978).

There is an important flaw in the partial-equilibrium approach to evaluating the distributive effects of pesticide regulation. While it offers a more reasonable approach to assessing distributional implications than the traditional partial-budgeting method, it provides only a limited, partial view of true distributional impacts. A complete distributional analysis would incorporate not only the direct effects of the regulation, but also all of the major indirect or spillover effects on related markets. If a detailed quantitative assessment of the major direct and indirect distributive effects of a pesticide restriction is desired, it would be necessary to conduct the distributive analysis in the context of multi-sector (or multi-crop) programming or econometric models. Of course, if the proposed regulation is expected to have only marginal yield or cost effects, the resultant spillovers will generally be negligible, implying that the partial-equilibrium estimates would be reliable.

The USDA/EPA benefit analysts currently have access to at least two complex mathematical models that can, in principle, reveal how regulatory decisions would impinge on the markets for certain major agricultural crops (namely, cotton, corn, barley, soybeans, oats, grain sorghum, and wheat). One of these models is a multi-crop linear programming model developed by EPA in the early 1970s to analyze some of the distributive effects of prohibiting the use of chlorinated hydrocarbon pesticides on corn (see Epp *et al.* 1977 for a more detailed description, especially pages 30–42). The second is a multi-crop econometric model recently developed for OPP by Lacewell and Taylor (described in Taylor *et al.* 1979). However, neither of these models is presently used by the USDA/EPA analysts in their benefit assessment work (A.L. Aspelin, OPP, EPA, Washington, D.C., personal communication, November 1978).

Reluctance to rely on the mathematical modelling approach to evaluate distributive effects of a pesticide regulation is justifiable. Frequently, the spillover effects of a proposed regulation are negligible and thus too small for mathematical models to detect with any degree of confidence (G. O'Mara, OPP, EPA, Washington, D.C., personal communication, June 1978). In addition, the generally poor quality of the cost and, especially, the yield data raises serious doubt as to the appropriateness of basing the benefit assessment on the results of sophisticated programming or econometric models. The detailed, seemingly precise results provided by the models may lend an unwarranted aura of credibility to the economic impact estimates. Consequently, if the mathematical modelling approach does become more important in the assessment of pesticide benefits, the Committee recommends that the analysts routinely report the results of sensitivity analyses in order to reveal the actual uncertainty surrounding the impact estimates.

In the qualitative discussions of the economic impacts of a regulatory action, the USDA/EPA analysts recognize the implications of conventional economic incidence analysis. They note, for example, that consumer prices are likely to rise following a regulatory response. However, the *quantitative* assessments usually assume that the burden of a regulatory decision will be borne entirely by the growers—or, more specifically, the users of the RPAR pesticide. Thus, the USDA/EPA quantitative benefit assessments tend to overstate the losses suffered by users of a cancelled (or otherwise regulated) pesticide. Similarly, they tend to understate the losses suffered by consumers and the gains enjoyed by nonusers. These inaccurate estimates arise mainly out of a failure to account explicitly for the output price changes likely to result from a regulatory action.

In connection with the estimation of the distributive effects, the USDA/EPA approach suffers from at least one other problem. Some of the distributive effects involve income *redistribution.* Crop price increases, for instance, will in large part redistribute purchasing power from consumers to growers. Thus, if increases in crop prices benefit growers by, say, $50 million annually, those same price increases cost consumers $50 million annually. (For simplicity, this statement ignores the likelihood that the higher prices will lead to greater production.)

Unfortunately, several of the benefit assessments have failed to spell out clearly the fact that gains to growers may entail losses for consumers. For instance, in the endrin/apple assessment (endrin is used in apple orchards to control voles) the following conclusion was reached regarding the likely impacts on apple growers:

> The greatest impacts will occur if current endrin users substitute zinc phosphide in their control programs. Under this program, current endrin users would incur losses in net returns equal to $19,110,000 after three years. Nonusers of endrin would experience increased net returns equal to $51,323,000 after three years due to higher apple prices caused by losses in the endrin use areas. Over the initial three-year period following the cancellation of endrin, users would experience a drop in net returns from $675 to $429 per acre, while nonusers would experience an average increase in net returns from $675 to $788 per acre.
>
> Under a CPN-DPN-herbicides-cultural methods program, the aggregate impacts upon users and non-users would be approximately one-half the magnitude projected under a Zn_2P_3 program. . . . [C]urrent endrin users would experience a loss in net returns of $9,479,000 over the initial three-year period. Non-users of endrin would receive an aggregate increase in net revenues of $25,773,000 over the same period (Luttner 1977c:76, 80).

In contrast, the analysis of the likely effect on consumers is essentially limited to the following:

> Although the cancellation of endrin has the potential to cause economic hardship for growers in the affected areas, the aggregate impact does not appear to be significant on a macroeconomic level (Luttner 1977c:84).

The reader should note that according to these three extracts, the net effect on the incomes of apple growers of suspending the use of endrin would be an increase of $32 million a year if zinc phosphide were substituted, or an increase of $16 million if CPN-DPN-herbicides were used. These figures give the misleading impression that there are no net benefits of using endrin in apple orchards, by including the gain to

TABLE 5.1 An Example of the Current Format for Reporting the Results of Benefit Assessments

Trifluralin Suspension on Cotton: Impact on Users and Nonusers Based on a 0.3 Price Elasticity for Domestic Demand

		Regions[a]				
Item	Unit	2	4	6	7	Total
Acres planted (1971-1976 average)[b]	1,000	785	4,138	1,444	5,591	11,958
Economic impact on trifluralin users						
Acres treated with trifluralin	1,000	432	3,724	1,083	3,075	8,314
Lint cotton production						
With trifluralin	Million lb	175	1,553	1,036	1,002	3,766
Without trifluralin	Million lb	171	1,514	811	696	3,192
Change in lint production	Million lb	4	39	225	306	574
Change in cottonseed production without trifluralin	Million lb	7	65	376	511	959
Reduction in income						
Added cost of weed control[c]	$ million	0.6	(−5.9)	7.4	3.8	5.9
Value of lost lint cotton[d]	$ million	2.4	23.4	135.0	183.6	344.4
Value of lost cottonseed[e]	$ million	0.4	3.2	18.8	25.6	48.0
Net reduction in revenue	$ million	3.4	20.7	161.2	213.0	398.3
Increase in income						
Gain from change in cotton price[f]	$ million	19.7	174.1	93.3	80.0	367.1

Cotton acres diverted to grain sorghum						
Decrease in variable costs[g]	$ million	—	—	—	16.0	16.0
Value of grain sorghum output[h]	$ million	—	—	—	38.8	38.8
Net increase in income	$ million	19.7	174.1	93.3	134.8	421.9
Net income change on trifluralin-treated acres	$ million	16.3	153.4	−67.9	−78.2	23.6
Economic impact on non-users of trifluralin from the change in cotton price[i]	$ million	—	—	—	—	188.3

[a] Region 2, Southeast; Region 4, Delta; Region 6, Southwest; Region 7, Southern Plains.

[b] Crop Production Annual Summary 1973 and 1976. USDA, Statistical Reporting Service CrPr 2-1 (74) and CrPr 2-1 (77).

[c] Difference between the trifluralin weed control program costs and the cost of the alternative weed control program.

[d] The base price for lint cotton was assumed to be $0.60 per pound.

[e] The price for cottonseed was assumed to be constant at $0.05 per pound.

[f] Production without trifluralin times $0.115 per pound. It was estimated that the price of cotton would increase from $0.60 to $0.715 per pound as a result of the reduced output.

[g] On the 307,500 cotton acres shifted to grain sorghum the savings in variable costs is $51.87 per acre. Variable costs for cotton were $109.29, and for grain sorghum, $57.42. Obtained from "Costs Producing Selected Crops in the United States—1975, 1976 and Projections from 1977," prepared by the Economic Research Service, USDA, for the Committee on Agriculture and Forestry, U.S. Senate, January 21, 1977.

[h] 53 bushels per acre times $2.38 per bushel (1973-1975 weighted average price) times 307,500 acres.

[i] Production on non-trifluralin-treated acres was estimated at 1637 million lb (1971-1976 average production of 5403 million lb minus 3766 million lb produced on trifluralin-treated acres). Increase in cotton price was estimated to be $0.115 per pound (footnote *f*).

Note: A dash indicates not applicable.
Source: USDA et al. (1977).

TABLE 5.2 An Example of the Recommended Format for the Presentation of Benefit Assessment Results

Cost of Denying Reregistration to Trifluralin for Use on Cotton (assuming demand elasticity is 0.3, horizontal supply curve)

	With Trifluralin	Without Trifluralin	($ Million)[b]
Real Costs of Denial			
Decrease in lint production 574 million lb at (0.60 + 0.715)/2			$377
Decrease in seed production 959 million lb at 0.05[a]			48
Value of substitute crop[a]			− 39
Added cost of weed control			6
Reduced variable cost on acres shifted to substitute			− 16
Total real costs			$376
Monetary Costs of Denial			
To trifluralin users:			
Lint production (million lb)	3766	3192	
Price	$0.60	$0.715	
Gross sales ($ million)	2260	2282	
Decrease in lint sales			−$ 22
Decrease in seed production[a]			48
Value of substitute[a]			− 39
Added cost of weed control			6
Reduced variable cost on acres shifted			− 16
Net monetary cost to users			− 23
To other cotton producers:			
Increase in gross sales 1637 million lb at $0.115			−$188
To consumers (foreign and domestic):			
Increased cost of output purchased 4829 million lb at $0.115			555
Loss in value from output restriction 574 million lb at (0.60 +0.715)/2 − 0.60 = 0.0575			33
			$588
Total monetary costs			$377

[a] Assumes change in output does not induce change in price.

[b] Negative entries indicate negative losses or gains.

Source: USDA et al. (1977, Table 1).

growers from the higher apple prices that would exist if it were not used, while ignoring the offsetting loss to consumers.

As a general rule, the USDA/EPA benefit assessments need to pay more attention to identifying implications of proposed regulations for the distribution of income. In many instances, the data are inadequate for measuring distributional effects with much precision. However, reasonable upper- and lower-bound estimates can usually be developed, for instance, by adopting assumptions about the plausible upper- and lower-bound values for demand and supply elasticities (see the chlorobenzilate analysis in Chapter 7 for an illustration).

A final recommendation concerns the presentation of results of benefit assessments. At present, no clear distinction is made in the benefit assessment documents between the real and pecuniary (or distributional) effects of not reregistering (or otherwise regulating) a pesticide. Not to distinguish carefully between them is confusing to trained readers and misleading to untrained readers.

An example of the type of format that is commonly used in reporting results of benefit assessments is provided in Table 5.1. According to the trifluralin assessment document (USDA *et al.* 1977), this table is supposed to present "the estimated short-run economic impact of a trifluralin suspension on cotton. . . . " Although the figures may be correct, the impression given by the table is entirely misleading.[3] According to the table, if trifluralin were banned, the net incomes of cotton farmers who use trifluralin would increase by $24 million a year (see the last column) and those of other cotton farmers would increase by $188 million for a total gain of $212 million in net farm income. As far as can be determined from the table, the American economy would be better off without trifluralin even apart from its effects on public health and the ecology. Of course, the facts are otherwise. If trifluralin is forbidden, more resources will be used to raise cotton and less cotton will be produced. As a result, purchasers of cotton will pay higher prices and receive less cotton.

A proper, "double-entry" accounting for the effect of banning trifluralin is shown in Table 5.2. The real resource cost entailed is constructed in the upper panel; it amounts to $376 million a year. The incidence of those costs is displayed in the lower panel. The monetary gains to cotton raisers are outweighed by the loss of $588 million sustained by cotton users. The net monetary loss ($588 - $212 = $376 million) is equal to the real resource cost. In this world every component of real cost is paid for by somebody.

The entries in the consumers category require a brief explanation. In connection with the first entry, the 4,829 million pounds of lint available without trifluralin would cost consumers $555 million more than that same quantity would cost at the price that would reign if trifluralin were available. In connection with the second entry, the $33 million measures the difference beween (1) the value consumers place on the 574 million pounds of lint that would be lost if trifluralin were suspended and (2) the value they place on the alternative commodities they can buy with the purchasing power released by the reduction in the quantity of lint demanded. The difference is nothing more than the consumers' surplus triangle discussed earlier in this chapter.

The display of separate real and monetary effects makes several things clear. First, the monetary effects are a distribution of the real effects. Apart from a rounding error in Table 5.2, the total of the monetary effects equals the total of the real effects. Second, in the present instance, the consumers sustain a loss that is more than 50 percent greater than the real loss. The reason is the assumed inelasticity of demand, which makes it possible for producers to more than shift their increased costs to consumers. The key figures, which are not found in the USDA/EPA presentation in Table 5.1, are that there would be a real loss measured by $376 million, which would result in a purchasing power loss of $588 million on the part of cotton users. (Note that in keeping with a preceding recommendation, these estimates should be reported as ranges, rather than as precise numbers.)

The Committee recommends that tables similar to Table 5.2 be routinely included in the benefit assessment reports.

NOTES

1. In economists' terms, this expression is the sum of the changes in producers' and consumers' surpluses. The measure provides an estimate of the unobservable sum of the compensating variations—the correct theoretical measure of changes in economic welfare. For a discussion of some of the technical problems associated with estimating welfare gains and losses with the producers' and consumers' surplus measures, see Chipman and Moore (1976, 1979), Mishan (1976), Mohring (1971), Silberberg (1972), and Willig (1976). As some of these authors note, there is considerable theoretical controversy as to whether consumer surplus has any meaning beyond the level of individual consumers.

2. In some instances, a restriction on a pesticide used in the production of commodity X (e.g., wheat) may indirectly affect the prices of other commodities (e.g., barley and oats) through demand or supply interdependencies. The benefit measure set forth as Equation 5.2 abstracts from the gains and losses that would be associated with such price changes. When the indirect price changes (and the related gains and losses) are important, allowance has to be made for them. Otherwise, the benefits will be incorrectly measured. However, in the Committee's opinion these indirect price effects will usually be small enough to neglect safely. The reasoning behind this belief is as follows. Most of these indirect gains and losses will be transfers of purchasing power between consumers and producers. While such

transfers may be relevant to an evaluation of the distributional consequences of a regulatory action, they are not relevant to an evaluation of the economic efficiency consequences of that action. In measuring the efficiency effects, it is necessary to account only for the *net* (or "deadweight") gains or losses in the other, related markets. The net gains or losses in these related markets appear likely to be small relative to the efficiency gains or losses in the primary market. In any event, the data will generally not permit quantification of either the gross or the net gains or losses associated with these market interdependencies.

3. The trifluralin estimates are used in this table merely for illustrative purposes; the Committee has not attempted to evaluate their accuracy.

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6 Evaluation of the Regulatory Options: Weighing the Risks and Benefits

INTRODUCTION

The ultimate goal of the RPAR process is to permit the Administrator to select the most desirable regulatory option, based on a weighing of the risks and the benefits of the various options. However, the risk and benefit analyses are, for the most part, conducted independently of one another. To facilitate the Administrator's selection of the "best" option, it is necessary to bring together in as intelligible a way as possible the main findings of the two independent analyses. The purpose of this chapter is to describe briefly the current approach to synthesizing and presenting the findings of the separate analyses and to recommend, where appropriate, some changes in that approach.

It should be clearly understood that benefit-risk analyses cannot decide which option to select. Even the most complete analysis will leave considerable room for judgment on the part of the responsible officials, beginning with the project manager. The analysis can only facilitate the decision.

DEVELOPING REGULATORY OPTIONS

CURRENT APPROACH

The development and evaluation of major regulatory options in pesticide (re)registration decisions is the purpose of the RPAR process. The primary responsibility for carrying out these activities rests with the project manager. Explicit guidelines for developing and evaluating regulatory options do not exist. Instead, general direction has been provided to the project manager in the form of a draft guidance package prepared by SPRD. The following is an excerpt from this material that is designed to aid the project manager in developing PD 3 (U.S. EPA 1978d):

> *Selection of Alternative Courses of Action*
>
> This section describes the risk/benefit approach taken to impact analysis. Initially, the analysis examines the adverse effects of risks associated with each existing use of the chemical. At the same time, information on the benefits (or the resultant effects from the removal of the chemical from the market) is being collected and analyzed. From this review, alternative actions are drafted and the new use patterns that would result from each action are examined. The risks and benefits of using substitute chemicals are also analyzed and incorporated into the alternative actions. Final alternative actions (major regulatory options) are then proposed and the risks are weighed against the benefits for each action (option).
>
> There are many components of Alternative Courses of Action: these are the various statutory and regulatory methods the EPA Administrator can utilize for restricting pesticide use under FIFRA. Some examples are changes in labeling, changes in classification, or cancellation. These components are affected by serious economic and social and/or environmental and health effect. It is important that these be mentioned generally. The difficulty of deciding which alternative actions are studied, can be emphasized through an explanation of the wide range of possibilities, i.e. the components mentioned above can be combined in numerous ways. Specifically, as the impact analysis is conducted on a use by use basis, the various regulatory and statutory methods of controlling pesticides can be applied to each use of a pesticide chemical, so that the number of possible alternative actions is sizable:
>
> cancel——variations——register
>
> The next portion of the PD 3 will list and discuss the alternative actions being considered as a result of the risk/benefit analysis. An explanation as to the reasons for the selection of the above alternative actions should follow. The rationale for developing the alternative actions may be somewhat standard in that generally, the effects of registering the pesticide (maintaining the status quo), the effects of cancelling the pesticide and the effects of restricting (using various methods) some uses of the chemical are considered. However, it is important that an explanation be provided as to why these alternatives were chosen, i.e. why certain regulatory and statutory methods were chosen and/or why certain substitute chemicals were chosen, as opposed to others. It would be helpful, if possible, to briefly mention some of the feasible alternatives that were not chosen as selected.
>
> *Review of the Impacts of Major Alternative Actions*
>
> This section of the PD 3 will discuss the impacts, beneficial and adverse, of the alternative actions chosen above as a result of the risk/benefit analysis. The

> secondary impacts, those associated with the use of substitute chemicals will be included. One way of presenting this information is in a form where the beneficial and adverse impacts are examined for environmental effects, health effects, economic effects and social effects. Important considerations for each category of effects are the short term and/or long term impacts, primary and/or secondary impacts and the irreversible and irretrievable impacts of the alternative action being discussed.
>
> A summary matrix of this information would be useful as it allows the reader to more easily envision the trade-offs between the risks and benefits in the decision process. Attachment 5 is an example of this type of matrix.[1] The matrix may be altered for each PD 3 depending upon the alternatives for the uses of each chemical. In addition to the summary matrix, a section of the text which compares the alternative actions would be helpful. This would simply be an explanation of the trade-offs between the risks and the benefits as depicted in the matrix.

Thus, the current methodology by which viable regulatory options are identified is somewhat vague. The basic approach to generating such options appears to be that of first listing on a use-by-use basis those options that would reduce potential exposures and then considering the attendant risks and benefits associated with them. In addition, other possible options that might be included have to do with requesting more data and delaying a decision, or making a temporary decision with the provision that further review will take place when additional data are available.

Some examples can serve to illustrate the current approach. For instance, PD 3 for chlorobenzilate simply states, "evaluation of the risk and benefit data suggests seven principal regulatory options" (U.S. EPA 1978a). Little more is said as to exactly how these major options were selected, although one infers that the selection process was accomplished through RPAR team meetings, the project manager's independent assessment and interpretation of team input, and limited internal review.

PD 4 for DBCP uses the "reduction of risk" as the rationale for developing major regulatory options (U.S. EPA 1978b, see especially section on Development and Selection of Regulatory Options). That is, options are generated in terms of whether they have the potential to reduce risk. If they do, the economic impacts of adopting the options are considered in a narrative fashion.

For the pesticide endrin, an early draft of PD 2/3 (Barbehenn 1978) suggests that to be viable a regulatory option must satisfy the following criteria:

> 1. It must yield an acceptable risk to benefit ratio from current use practice(s) or improve the risk to benefit ratio with additional options considered;

2. It must be a technically and economically feasible regulation from the perspective of user groups;
3. It must be consistent with the authority of the Agency;
4. It should be enforceable; or
5. If enforcement is difficult to achieve, then a high degree of compliance to the regulation by users must be expected.

It should be clear from these examples that the relatively loose guidance provided in developing regulatory options will mean that considerable discretion is left to project managers as chief authors of PD 3's.

RECOMMENDATIONS

In developing regulatory options, the Committee recognizes the difficulties associated with balancing the need to maintain benefits of pesticide use, for example increased crop production, with the need to protect human health and ecosystems. At the same time, the Committee acknowledges that each compound that undergoes the RPAR process will have certain unique characteristics; hence, the development of relevant regulatory options may not be easily generalized. Nevertheless, it is worth highlighting at least two broad recommendations.

First, the Committee thinks that it is important that the major regulatory options be generated at an early stage in the process to ensure that necessary analyses of both the compound under review and its substitutes will be carried out in a timely fashion. An important consequence of early generation of regulatory options should be that their implications on the use of alternative pesticides will be seen and taken into account early in the process (see Chapter 3, section on Modification to the Preliminary Ranking: The Role of Alternative Pesticides).

Second, the Committee thinks that one of the criteria listed above from the early endrin PD 2/3 is worthy of further emphasis, namely, that in developing regulatory options adequate weight should be given to enforceability. It is meaningless for the Agency to put forth a regulation that would reduce risk if it will not be respected and cannot be enforced. For example, with regard to the protection of pesticide applicators, questions have arisen over whether clothing and respirator requirements are enforceable. If such restrictions cannot be enforced, then the "real" risk reductions associated with these protective measures will be overstated and, more importantly, the final regulatory decision that is chosen may not be the correct one.

Basically, the Agency has the responsibility for providing adequate justification of its development of the major regulatory options that it will evaluate.

SELECTION OF REGULATORY OPTIONS

CURRENT APPROACH

The portion of a PD 3 entitled, "Review of the Impacts of Major Alternative Actions," presents the evaluations of the major regulatory options. The format used to report this material involves enumerating the options and discussing them one by one in terms of the expected risks and benefits that would result if the option were adopted by the Agency.

In many cases, descriptions of risk are given in terms of quantitative estimates of lifetime risk, margins of safety, or expected wildlife losses; in other instances, the descriptions involve qualitative statements as to how specific options would be likely to reduce risk. Risks associated with alternative pesticides that may come into use are rarely quantified because of lack of data. On the other hand, economic impacts (or benefits) are usually described more quantitatively.

In addition to narrative descriptions that discuss the trade-offs between the risks and benefits associated with each major regulatory option, the draft guidance package provided by SPRD (and quoted above) suggests that the information be displayed in matrix form. The purpose of such a matrix presentation is to make the inherent trade-offs associated with each major option readily apparent to the decision maker.

An example will illustrate this approach, which has been used by the Agency in most of the PD 3's. In the chlorobenzilate PD 3, the seven regulatory options that were considered are as follows (U.S. EPA 1978a):

A. Continue Registration of All Uses.
B. Cancel All Uses.
C. Continue Registration of Chlorobenzilate Use on Citrus and Amend the Terms and Conditions of Registration; Cancel All Other Uses.
D. Cancel Chlorobenzilate Use on Citrus to Take Effect After Five Years, and in the Interim Amend the Terms and Conditions of Registration; Cancel All Other Uses.
E. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration, Require That Identified Exposure Data Be Submitted to EPA in 18 months; Reevaluate the Use on Citrus After Additional Exposure Data Become Available; Cancel All Other Uses.
F. Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas,

and California, Amend the Terms and Conditions of Registration, Require that Identified Exposure Data be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Become Available; Cancel Use on Citrus in Arizona and All Other Uses.

G. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration; Prohibit the Use of Pulp from Chlorobenzilate-Treated Citrus and Cattle Feed; Establish Complementary Tolerances; Cancel All Other Uses.

Once the options were identified, their associated risks and benefits were presented, first in tabular form and then in narrative fashion. Tables 6.1 and 6.2 reproduce the relevant tables from PD 3 for chlorobenzilate. Following these tables in the PD 3, discussions of each option were presented, describing the implications of choosing one option over another. The next section of the position document presented the recommended regulatory action, Option F (U.S. EPA 1978a:88). (In PD 4 for chlorobenzilate, the Agency modified Option F and allowed continued registration in Arizona.)

While a matrix or tabular format is generally used to summarize results from the risk and benefit analyses, other approaches are not uncommon. For instance, the endrin PD 2/3 (U.S. EPA 1978c) presents the findings and discusses the implications of the various regulatory options in narrative fashion only. No tables, graphs, or charts were used in the endrin PD 2/3 to consolidate and summarize the results for easy access by the decision maker (or other interested parties).

RECOMMENDED APPROACH

All the work discussed in the preceding two chapters and the first half of this one leads up to the selection of the best of the regulatory options that have been identified. At this stage, estimates are available of the risks—in terms of human exposure estimates and the relative potency of the compound—imposed by each use of the pesticide under each of the regulatory options. Corresponding estimates of the benefits yielded by each of the uses permitted by each option are also available. Finally, in accordance with Chapter 3, there are comparable estimates of the risks and benefits of the alternative pesticides that are likely to be used if the pesticide under review is restricted or denied reregistration. It remains to put these data together and evaluate the result.

The first stage is to estimate the risks and the economic impacts that would result from adopting each option. The risk imposed by an option is the sum of the risks entailed by all the uses that it permits. This summation has to be performed separately for each kind of risk and each exposed population. For example, if one option permits a pesticide to be used on 10 different food crops, the risk of increased cancer incidence to the general U.S. population from dietary exposure would be estimated as the sum of the amounts of the pesticide ingested by a typical consumer in the form of residues on all those foods, taking account of the carcinogenic activity of the pesticide. If an alternative option forbids the use of the pesticide on five of the foods, the dietary risk to a typical member of the population would be estimated as the total ingestion of residue on the five permitted foods plus the equivalent intake of alternative pesticides, if any, used on the five forbidden foods in response to this stricter regulation, again taking account of the carcinogenic activity of the pesticide. (The equivalent intakes would be estimated from the CAI's by the methods discussed in Appendix B.) Such an aggregate risk would be computed for each option for each population and type of hazard imposed by the uses the option permits. For example, risk to applicators would be computed separately from risk to a population consuming residues on or in food; risk of cancer would be computed separately from risk of abnormal offspring, acute toxicity, and so on. Risks are calculated as lifetime values, taking the economic life of pesticides into account.

The economic impact or cost of a regulation is also a sum, taken over all the uses that it restricts or prohibits. The component of the aggregate cost arising from each use is the forgone benefits discussed in Chapter 5. That is, it is the excess of the surpluses or net benefits that would be enjoyed without the regulation over the net benefits yielded by the methods of operation that would be resorted to in response to the regulation. Costs of administration and enforcement (both public and private) should be added to this sum to obtain the total cost of the regulation. Costs are calculated as discounted present values over the remaining economic lifetime of the pesticides.

When the risks and the costs of all the regulatory options have been estimated in this manner, nothing remains but to compare the performances of the different options and select the one that appears best, all things considered. Unfortunately, this final comparison is a very difficult task. Three great problems have to be solved in order to perform it. First, there is the problem of the incomparability of the units in which risks and costs are expressed and the additional complexity introduced by having to deal with different types of risk. Second, there is the uneven distribution of risks and costs over different portions of the population. Third, there are the uncertainties surrounding the data and the estimates on which decisions must rest. These are very pervasive problems, common to many of the decisions that EPA has to make and often

TABLE 6.1 A Sample of the Current Format Used by the Office of Pesticide Programs to Display the Results of Risk Assessments by Regulatory Option

Regulatory Options and Maximum Risk Incidence from Chlorobenzilate Use

Option	Florida Citrus Consumers	Remainder of U.S. Citrus Consumers	Citrus Pesticide Applicators	Florida Citrus Pickers	Noncitrus Use Consumers	Noncitrus Pesticide Applicators	Noncitrus U.S. Pickers
A. Continue registration of all uses	2.6-6.4 per million	2.0 per million	400-1400 per million	No data	0.1 per million	No data	No data
B. Cancel all uses	0	0	0	0	0	0	0
C. Continue registration of chlorobenzilate uses on citrus and amend the terms and conditions for registration; cancel all other uses	2.6-6.4 per million	2.0 per million	4-278 per million	No data	0	0	0
D. Cancel chlorobenzilate use on citrus to take effect after 5 years and in the interim amend the terms and conditions for registration; cancel all other uses	0.2-0.5 per million	0.1 per million	0.3-20 per million	Reduced exposure	0	0	0

E. Continue registration of chlorobenzilate use on citrus, amend terms and conditions of registration, request that identified exposure data be submitted to EPA in 18 months; reevaluate the use of citrus after additional exposure data become available; cancel all other uses	2.6-6.4^a per million	2.0^a	4-278^a per million	No data	0	0	0
F. Continue registration of chlorobenzilate use on citrus in Florida, Texas, and California; amend terms and conditions of registration, require that identified exposure data be submitted to EPA in 18 months; reevaluate the use on citrus after additional exposure data become available; cancel use on citrus in Arizona and all other uses	2.6-6.4^a per million	Marginal risk reductions for consumers coincident with an approximate 3000-acre reduction in use, applicator risk in Arizona eliminated—		No data	0	0	0

TABLE 6.1 (*continued*)

Regulatory Options and Maximum Risk Incidence from Chlorobenzilate Use

Option	Florida Citrus Consumers	Remainder of U.S. Citrus Consumers	Citrus Pesticide Applicators	Florida Citrus Pickers	Noncitrus Use Consumers	Noncitrus Pesticide Applicators	Noncitrus U.S. Pickers
G. Continue registration of chlorobenzilate use on citrus; amend the terms and conditions of registration; prohibit the use of pulp from chlorobenzilate-treated citrus as cattle feed; initiate action for EPA to establish a tolerance on chlorobenzilate residue in citrus pulp; cancel all other uses	2[b] per million	2[b] per million	4-278[b] per million	No data	0	0	0

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[a] Additional data may result in regulatory action reducing risk below these estimates.
[b] Assume that this approach will not create a de facto cancellation; if the market forces a de facto cancellation risks are zero in every case.

Source: U.S. EPA (1978a).

TABLE 6.2 A Sample of the Current Format Used by the Office of Pesticide Programs to Display the Results of Benefit Assessments by Regulatory Option

Economic Impacts Resulting from Chlorobenzilate Regulatory Options

Option	Commodity	Economic Impact[a]					
A. Continue registration of all uses	Citrus	None					
	Cotton	None					
	Fruits/nuts	None					
B. Cancel all uses	Citrus	Area	Economic Impact in Years After Cancellation ($ thousand)				
		AZ	0	0	0	0	0
		CA	600	1,600	2,400	3,100	3,700
		FL	12,200	20,800	28,300	34,600	40,100
		TX	300	300	200	200	200
		US	13,000	22,600	30,900	37,900	44,000
		and thereafter[b]					
		$4.4-$19.1 million for amended use direction[c]					
	Cotton	$125,000/year					
	Fruit/nuts	$69,000/year					
C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions for registration; cancel all other uses	Citrus	$4.4-$19.1 million for amended use direction[c]					
	Cotton	$125,000/year					
	Fruits/nuts	$69,000/year					

TABLE 6.2 *(continued)*

Economic Impacts Resulting from Chlorobenzilate Regulatory Options

Option	Commodity	Economic Impact[a]					
D. Cancel chlorobenzilate use on citrus to take effect after 5 years and in the interim amend the terms and conditions for registration; cancel all other uses	Citrus	No impact years 1-5					
		Area	Economic Impact in Years After Cancellation ($ thousand)				
		AZ	0	0	0	0	0
		CA	400	1,100	1,800	2,100	2,500
		FL	8,700	14,800	20,000	24,600	28,500
		TX	200	200	200	300	300
		US	9,300	16,100	22,000	27,000	31,300
		and thereafter[b] $4.4-$19.1 million for amended use direction[c]					
	Cotton	$125,000/year					
	Fruits/nuts	$69,000/year					
E. Continue registration of chlorobenzilate use on citrus, amend the terms and conditions for registration, require that identified exposure data be submitted to EPA in 18 months; reevaluate the use on citrus after additional exposure data become available; cancel all other uses	Citrus	$4.4-$19.1 million for amended use direction[c] Potential for additional impacts dependent on test results					
	Cotton	$125,000/year					
	Fruits/nuts	$69,000/year					

F. Continue registration of chlorobenzilate use on citrus in Florida, Texas, and California; amend terms and conditions of registration, require that identified exposure data be submitted to EPA in 18 months; reevaluate the use on citrus after additional exposure data become available; cancel use on citrus in Arizona and all other uses	Citrus	$4.4-$19.1 million for amended use direction[c]				
		Arizona—no economic impact potential for additional impacts dependent on test results				
	Cotton	$125,000/year				
	Fruits/nuts	$69,000/year				
		Economic Impact in Years After Cancellation ($ thousand)				
G. Continue registration of chlorobenzilate use on citrus, amend the terms and conditions of registration, prohibit the use of pulp from chlorobenzilate-treated citrus as cattle feed; initiate action for EPA to establish a tolerance on chlorobenzilate residue in citrus pulp; cancel all other uses.	Citrus	0	0	0	0	0
		600	1,600	2,400	3,000	3,700
		12,200	20,800	28,300	36,600	40,000
		300	200	200	200	200
		13,000	22,600	30,900	38,000	44,000
		and thereafter[b,d]				
		$4.4-$19.1 million for amended use direction[c]				

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[a] All future dollar impacts are given in present values. The citrus cancellation impact in year 1 ($13,000,000) is of the same magnitude as the first-year impact if it is delayed until the sixth year ($9,322,000). However, the discounting factor reduces present value of the sixth-year impact relative to the first-year impact.

[b] Assumes no establishment of viable substitute compatible with integrated pest management (IPM) and at cost approximately equivalent to chlorobenzilate's.

[c] Protective clothing cost for applicators was assumed to be negligible (respirators $15 each). Enclosed cab costs range from $4,250 (cab purchase) to $18,290 (new tractor with cab). A total of $4.4-$19.1 million for 1,045 applicators, depending on whether tractors are adapted or replaced, would be the maximum potential capital outlay. These capital outlays are for air-conditioned cabs; the cost estimates do not reflect the use of positive-pressure air filtration systems.

[d] Assumes loss of feedstuff market will cause growers to cease using chlorobenzilate; if not then same impact as Option C.

Source: U.S. EPA (1978a).

encountered in other government agencies and the private business sector as well. They have given rise to a substantial literature called decision theory.[2] Our recommendations take advantage of many of the insights developed in decision theory. We do not believe, however, that it is practicable for OPP to ascertain the "preference functions" or "objective functions" required by a full-blown decision analysis. We shall therefore recommend below a simplified, more *ad hoc* procedure.

In practice, all three of the problems listed above have to be confronted simultaneously in selecting the best regulatory option. For purposes of discussion, however, the issues raised by each of the difficulties can be perceived most clearly if they are considered one at a time.

To this end, let us suppose temporarily that there are no uncertainties, so that the risks and costs of the different options are known exactly and with complete reliability. We further suppose, temporarily, that no distributional considerations or problems of equity affect the relative desirabilities of the different options. And further, to begin with, we suppose that the only consequences relevant to the choice are the costs of the alternative options, derived in accordance with the methods discussed in Chapter 5, and the effects on the incidence of cancer, expressed by CAI's and estimates of the amounts of the chemical to which different segments of the population are exposed, as discussed in Chapter 4 and Appendix B.

Under these stringent assumptions, all the data relevant to the decision can be exhibited on a single chart similar to the one shown as Figure 6.1. The exposure and cost data underlying Figure 6.1 are shown in Table 6.3. Figure 6.1 shows the potential consequences of adopting five available options (labeled A through E) for the regulation of a mythical pesticide called Pestide. The horizontal axis measures cost (i.e., benefits of Pestide use forgone by regulation plus regulatory costs) in millions of dollars as discounted present values over the remaining economic lifetime of Pestide. There are five vertical lines, one for each option, placed at the abscissas that correspond to the discounted cost of the option. (Disregard the right-hand scales for the moment.) The left-hand scale, calibrated in micromoles per kilogram, measures lifetime doses of Pestide, including the Pestide-equivalent doses of alternative pesticides that are likely to be used under the various options. Two curves, or rather broken lines, are shown, one for the U.S. population in general and one for a special exposure group showing the change in dose and cost as one moves through the options from A to E. Thus, if Option A represents the status quo, its cost is zero, it exposes the general U.S. population to lifetime doses of 0.68 μ moles/kg of Pestide, and the

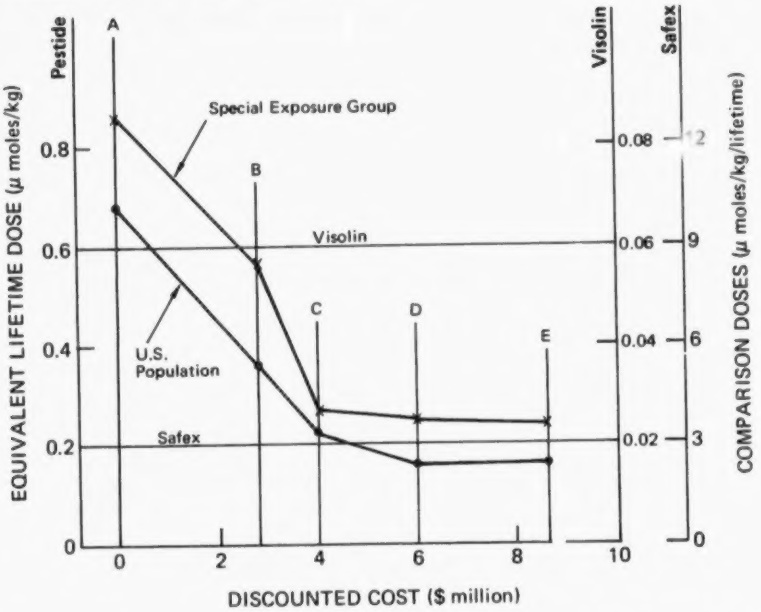

FIGURE 6.1 Equivalent lifetime doses and discounted costs of five options for regulating Pestide, with carcinogenic reference compound doses: certainty case (see text for discussion). Source: Table 6.3 and text.

special exposure group is exposed to lifetime doses of 0.86 μ moles/kg. As the chart is read from left to right, the same three data are shown for the other four options in order of their costliness.

We can now introduce the right-hand scales. The first relates to a mythical comparison compound, Visolin, about which two things are known. First, the CAI of Visolin is 10 times that of Pestide. (Again, it is assumed for the sake of simplicity that all CAI's are known precisely.) Accordingly, the lifetime dose scale for Visolin is one tenth the scale for Pestide indicating, for example, that 0.06 μ moles/kg of Visolin produces an effect comparable to 0.6 μ moles/kg of Pestide. Second, Visolin was denied reregistration on the basis of analyses that indicated that if it had been reregistered, a significant population group would have been exposed to lifetime doses of 0.06 μ moles/kg of Visolin. This fact is recorded by the horizontal line labeled Visolin at that dose level.

The right-most scale relates to Safex, another mythical comparison

TABLE 6.3 Equivalent Lifetime Doses and Discounted Costs of Five Options for Regulating Pestide

	Regulatory Option				
	A	B	C	D	E
Cost ($ million)					
Minimum-plausible	0	2.5	3.0	4.0	7.0
Probable	0	2.8	4.0	6.0	8.6
Maximum-plausible	0	4.0	5.5	7.5	10.0
Equivalent lifetime doses (μ moles/kg)					
U.S. population					
Probable	0.68	0.36	0.22	0.16	0.16
Maximum-plausible	1.9	1.2	0.57	0.35	0.35
Special exposure group					
Probable	0.86	0.56	0.27	0.25	0.24
Maximum-plausible	2.4	2.0	0.70	0.58	0.55

compound. Its CAI is one fifteenth of Pestide's, so that its scale is the same as Pestide's mutiplied by 15. Safex was reregistered and the supporting risk analyses showed that the greatest lifetime dose to which any large population group would be exposed was in the neighborhood of 3 μ moles/kg. This fact is shown by the horizontal line labeled Safex.

With this chart in hand, the RPAR team or the Administrator might reason as follows: if Pestide is reregistered according to Option A, both the general population and the special exposure group would be exposed to lifetime doses greater than the one equivalent to the potential exposure to Visolin that led to the denial of its reregistration. That is, the general population would receive an estimated lifetime dose of 0.68 μ moles/kg, the special exposure group would receive 0.86 μ moles/kg, and the Pestide equivalent of the Visolin dose level at which Visolin was cancelled is 0.6 μ moles/kg. Since the risks at 0.6 μ moles/kg (Pestide equivalent) were unacceptable in the Visolin case, Option A can be eliminated (ignoring the benefits of Pestide use versus those of Visolin use). Under Option B, both groups are exposed to doses below the Pestide cut-off point suggested by the Visolin precedent. But—violating slightly our assumption of complete certainty—suppose the special exposure group is not sufficiently below the cut-off point and Option B cannot be regarded as entirely safe for it. Besides, Option C costs only $1.2 million more than B and provides significant reductions in the doses received by both groups. Options D and E cost considerably more than

C ($2 and $4.6 million, respectively) without affording substantial reductions in the doses to which the special exposure group will be exposed. Although there is greater improvement in the exposure of the general population between Option C and Options D and E than for the special exposure group, under Option C the general U.S. population is already virtually at the level that was found to be acceptable in the Safex case. So, all in all, Option C appears to be the wisest course to follow.

It has to be concluded that such reasoning is subjective and far from rigorous. For one thing, the risk estimates on which the Visolin and Safex cut-off points were based may have used numerical estimates of morbidity or mortality derived from animal-to-human extrapolations. Further, the above reasoning ignores the costs that society (embodied by the decision maker) was willing to incur to avoid continued Visolin exposure or unwilling to incur in the case of Safex. For example, it may have happened that Visolin was denied reregistration at a dosage level of 0.06 μ moles/kg per lifetime in large part because benefits from continuing to use it were estimated to be very small, and that Safex was reregistered at a dosage level of 3 μ moles/kg per lifetime because it was virtually essential to the profitable production of an important crop.

In some cases, suitable comparison compounds can be found for which benefit-risk analyses have been conducted to determine the dose level where risks are considered to balance benefits. An example of such an instance might be the interim drinking water standard for trihalomethanes (U.S. EPA 1978e), where the costs of treatment techniques for achieving a maximum contaminant level of 0.10 mg/l were balanced against human health considerations (in particular, excess risk of cancer). Such considerations, if known, are clearly relevant to the decision under consideration. It is also most useful to a decision maker if the comparison compounds provide an upper and lower bound in terms of equivalent doses. Even in the highly simplified and idealized circumstances of the Pestide example, however, the kinds of data that risk and benefit analyses can provide are in principle not sufficient to determine the decision or to identify the best option. In the end there is inevitably considerable scope for judgment and discretion.

To advance one step up the ladder of complexity, we can now admit that in many instances there will be several types of effects to be taken into account in addition to costs. For example, the risk of fish kills may be a matter of concern in addition to cancer risk, and other health and environmental effects may be relevant also. In such cases, it may not be possible to pack all the pertinent data onto a single chart (although various health effects can be introduced by adding right-hand scales based on appropriate potency indexes). It may be feasible to use a single

TABLE 6.4 Changes in Discounted Costs, Equivalent Lifetime Doses, and Environmental Risks for Alternative Regulations of Pestide: Certainty Case

	Change in Regulation			
	Option A to Option B	Option B to Option C	Option C to Option D	Option D to Option E
Increase in cost ($ million)	2.8	1.2	2.0	2.6
Decrease in equivalent lifetime doses (μ moles/kg)				
U.S. population	0.32	0.14	0.06	0
Special exposure group	0.30	0.29	0.02	0.01
Decrease in number of fish killed (1000/yr)	16	22	0	0

Source: Table 6.3 and text.

table. A particularly helpful table is one that shows incremental changes, that is, one that shows the changes in costs, lifetime doses to which relevant population groups are exposed, and say, the number of fish killed as one moves from one option to the next most costly one. Table 6.4 illustrates such a table. Although this particular example does not identify the type or potency of the health hazards, it does show at a glance that Option B affords substantial improvements over Option A with respect to all exposed groups, and that Option C offers similar gains over Option B. But thereafter, moving from Option C to Option D and then to Option E would impose substantial costs without corresponding improvements in any of the dosages or impacts on fish.

The form of presentation is not our concern, however. Our concern is to emphasize the need for judgment when diverse health, environmental, and economic effects have to be taken into account. The basic considerations remain the same no matter how many different effects are relevant, but the difficulty of arriving at a decision generally increases with the number of relevant kinds of effects. Peeling the onion layer by layer is a natural and frequently helpful decision strategy. A preliminary selection of a regulatory option might be made by charting only the most significant type of risk (as in Figure 6.1). This selection can then be reviewed by comparing its impact on the second most important type of risk with the impacts of the other admissible options—that is, options that do not lead to unacceptable dose levels for any type of risk—and so on, down the list. In practice, fortunately, it appears that the selection of regulatory options for pesticides generally depends on only one or two kinds of risk of preponderant importance, in addition, of course, to costs. Keeney and Raiffa (1976) deal at length with methods for choosing preferred options when numerous consequences, or attributes, have to be taken into account. Some helpful suggestions, expressed less technically, can be found in Stokey and Zeckhauser (1978).

We can now introduce the second great obstacle, considerations of equity and distribution. They enter because the costs of the alternative options will fall unequally on different segments of the population and the risks will also be distributed unevenly. In a sense, distributional issues do not add methodological complications, since analyzing the impacts of different options on different segments of the population is conceptually akin to analyzing the different, incommensurable types of consequence that have just been discussed. In fact, the distribution of risks is already considered, since different types of risk and affected populations are assessed separately. But distributional effects such as abrupt changes in the competitive positions of different agricultural regions may also merit separate analyses. Additional charts and tables may be required to compare the risks and costs for specific population groups that are particularly affected by adopting certain regulatory options. These narrowly focused analyses may well preclude an option that appears attractive on the basis of the more aggregate evaluations, or they may suggest the desirability of modifying options to reduce the economic burden on some population groups. The analyses of both changes in risks and costs should therefore take great care to identify segments of the population (or regions) that are particularly affected by the regulatory options and to estimate the risks and costs imposed upon them, so that the data needed for disaggregated evaluations are at hand.

The third great obstacle is the substantial degree of uncertainty and approximation surrounding all the data and estimates, both risk and benefit, that are available in practice. To introduce this complication we can revert to the example of the Pestide decision. Because the consequences of the alternative regulatory options are now uncertain, there are more data to be assimilated than can be presented on a single chart, so two are used.

The first chart, Figure 6.2, compares the estimates of probable lifetime doses resulting from the various options with estimated ranges of their costs. The probable lifetime doses in this chart should represent the analyst's best judgment of the doses likely to be received by typical members of the populations considered. Option A, whose costs are known to be zero without any range of uncertainty, is represented by two points, the higher one corresponding to the probable lifetime dose received by members of the special exposure group and the lower one to the corresponding dose that would be received by members of the general U.S. population. Because of the uncertainties in the subsequent options, however, the costs can no longer be depicted as vertical lines. Each of the other options is represented by two line segments, each extending horizontally from the lowest cost believed to be likely to the maximum-plausible cost. The higher segment is placed at the dose level estimated to be most probable for the more exposed population group and the lower line segment is at the most probable dose level for the population in general. The Visolin cut-off line is again shown for reference. However, the uncertainty in the CAI values used to calculate the Pestide-equivalent dose of Visolin (see Chapter 4 and Appendix B) now shows on Figure 6.2 as a horizontal band around the 0.06 μ mole/kg level. Things neither appear to be, nor are, as simple and clear in this figure as they were in the previous one. Still, if one traces through the sequence of line segments corresponding to each of the population groups, the same reasoning as was used before can be invoked and Option C again stands out as the most appealing of the alternative options.

The second chart, used in the case of uncertain estimates, compares the maximum-plausible doses to be expected under the different options with the estimated ranges of costs. This comparison, shown as Figure 6.3, has the same structure and scales as Figure 6.2 and is intended to be comparable with it: there are only two differences. First, the line segments for the different options are now plotted at ordinates that correspond to the maximum lifetime doses believed to be at all plausible under those options; the abscissas or range of costs remain the same. Second, there are two horizontal bands for the comparison compound, Visolin. The lower one is the familar Visolin cut-off. Notice that if this band were interpreted in the way it was on the previous chart, Option C would no longer be admissible, since there is some possibility that under it the members of the special exposure population will receive greater lifetime doses of Pestide than comparison with the Visolin decision indicates to be acceptable. But it is not entirely reasonable to compare the worst-case results of Pestide regulation with the probable-case results of Visolin regulation. Therefore, a band has been added at the level of the maximum-plausible dose estimated to result from using Visolin. This band appears around 0.15 μ moles/kg of Visolin. The possibility of exposing people to such high dosages may well have had more influence on the Visolin decision than the much lower probable estimate.

This additional band reduces but does not eliminate the difficulty of

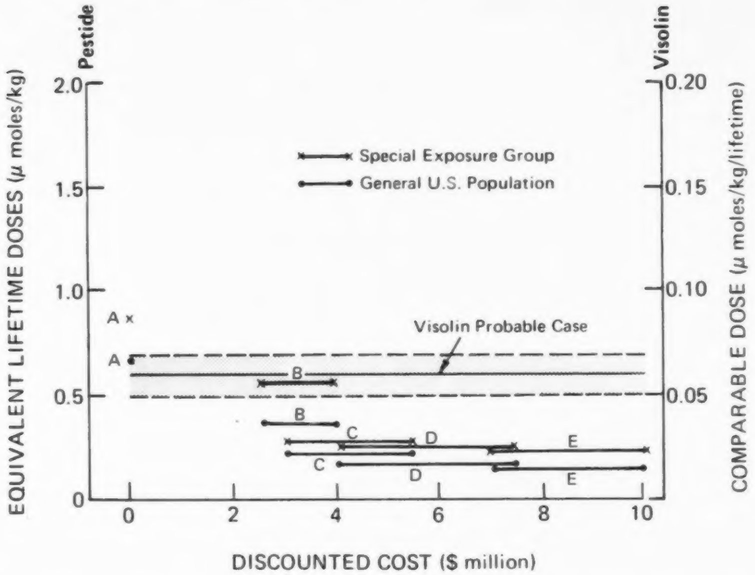

FIGURE 6.2 Equivalent probable lifetime doses and ranges of discounted costs of five options for regulating Pestide; carcinogenic reference compounds included (see text for discussion). Source: Table 6.3 and text.

arriving at a decision on the basis of Figures 6.2 and 6.3. Option C still appears attractive, but two judgments must be made about it. First, it must be decided whether the (perhaps slight) possibility that the special exposure population would receive greater doses of Pestide than are comparable to the forbidden doses of Visolin is acceptable, given the cost advantage of Option C over Option D (which is by no means assured, since the line segments overlap horizontally; see Figure 6.3). Notice that Option D offers only a modest reduction in the probable dose over Option C (Figure 6.2). Second, it must be determined if it is likely that the Agency will face serious criticisms politically if Option C is adopted and the resulting doses actually materialize at or near the maximum-plausible estimates. There is an unfortunate asymmetry here. If Option D is selected, when in fact the probable estimate is close to the mark, no one will ever know that Option C would have been acceptable risk-wise and less expensive, nor will anyone charge EPA with wasting resources on overly cautious decisions. But if Option C is chosen, and the

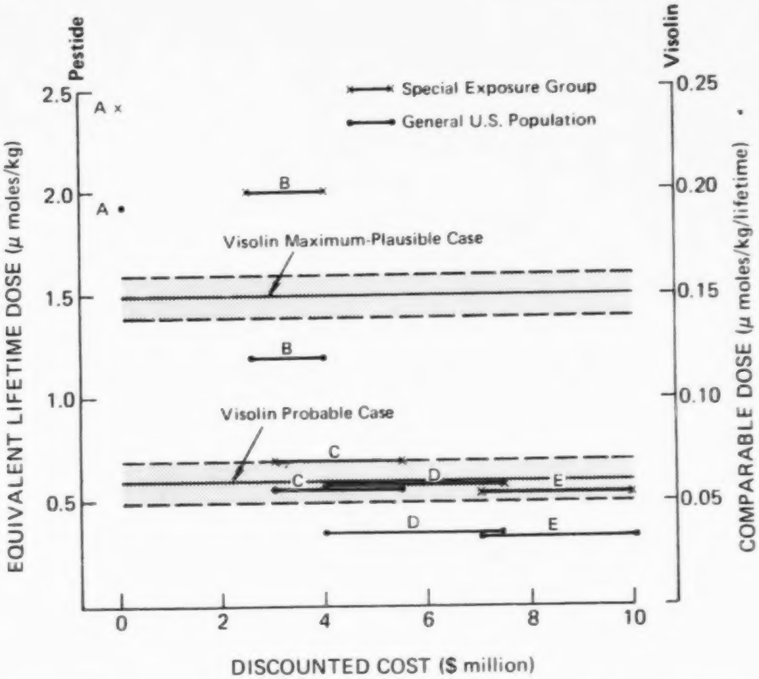

FIGURE 6.3 Equivalent maximum-plausible lifetime doses and ranges of discounted costs of five options for regulating Pestide; carcinogenic reference compounds included (see text for discussion). Source: Table 6.3 and text.

populations then receive doses close to the maximum-plausible estimate, severe criticism is likely to ensue. In the Committee's view, this asymmetry creates an incentive for the Agency to pay more attention to worst-case estimates than is consistent with the judicious use of economic resources. The Committee sees no way to reduce this bureaucratic bias other than to point it out.

The three difficulties that have just been discussed—the incomparability of risk and cost units, uneven distribution of risks and costs, and substantial uncertainty in the data and subsequent estimates—make the selection among regulatory options truly difficult and perplexing. The decisions can be made somewhat less baffling if decision makers are conscious of the sources of the difficulties and if analysts approach the problem in the spirit illustrated by the Pestide example. But in many instances, there is no "trickery" that can make the decision easy. Subjective judgment and discretion will always be required.

NOTES

1. See Tables 6.1 and 6.2.

2. For a general discussion of decision analysis see Howard (1966). The leading treatise on the three problems now being discussed is probably Keeney and Raiffa (1976). It is not easy reading. It contains an extensive bibliography that covers most aspects of these problems.

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7 Application to Chlorobenzilate

INTRODUCTION

The preceding chapters have reviewed the methods currently used by the OPP in selecting pesticides for review and in analyzing the benefits and risks of alternative regulatory measures where they appear appropriate. A number of important recommendations for revising these procedures have also been made. But it is easier to recommend than to perform. Therefore, the Committee has felt responsible for applying its recommendations to an actual instance, to the extent that its resources permitted. This chapter reports on that application. It will also serve to help clarify the Committee's recommendations by illustrating how they are implemented.

Chlorobenzilate was selected as the pesticide for the test application. It was the first pesticide to complete the entire RPAR procedure and, consequently, all the data used in EPA's evaluation were readily available for the Committee's use and appraisal. Because OPP has previously completed benefit and risk assessments for chlorobenzilate, including a comparison of benefits and risks associated with various regulatory options (U.S. EPA 1978a, 1979), the discussion in this chapter is to some extent framed in terms of a critique of the OPP analysis. The structure of the chapter basically follows the format of OPP's *Chlorobenzilate: Position Document 3* (U.S. EPA 1978a). The first section reviews chemical and physical properties, registered uses, and environmental fate of the compound. The second and third sections present the Committee's risk and benefit assessments, respectively. Finally, in the last section, benefits and risks are compared and presented in a manner that reveals not only the Committee's assessment of the trade-offs for the major regulatory options considered by OPP, but also the uncertainty in the scientific base and the extent to which value judgments enter into the decision. This chapter focuses on recommended departures from OPP's analytical methodology; it is not intended to stand as an independent document on chlorobenzilate.

BACKGROUND

Chlorobenzilate (ethyl 4,4′-dichlorobenzilate), a chlorinated hydrocarbon acaricide, is manufactured by esterification of dichlorobenzilic acid and is formulated principally as emulsifiable concentrates and wettable powders (Severn 1978). The formulation marketed in the United States contains 45.5 percent technical-grade chlorobenzilate. Approximately 93 percent of this amount is pure chlorobenzilate; the remaining 7 percent consists of several unidentified intermediates and other impurities (U.S. EPA 1978b).

Chlorobenzilate is registered for use on almonds, walnuts, apples, melons, cherries, citrus fruit, cotton, pears, ornamentals, and trees (U.S. EPA 1978a). Approximately 90 percent of the total amount used in the United States is applied to citrus to control the citrus rust mite (U.S. EPA 1978a); the principal crops on which chlorobenzilate is applied are oranges, grapefruits, and lemons (Luttner 1977a). Limited use also occurs on limes, tangerines, and tangelos (Lutter 1977a). The predominant method of applying chlorobenzilate to citrus groves is with a speed sprayer pulled by a tractor. The illustrative analysis in this chapter concentrates on the principal uses of chlorobenzilate, namely, mite control on oranges, grapefruits, and lemons.

PROPERTIES OF CHLOROBENZILATE, ETHION, AND DICOFOL

As noted earlier, to assess the risks and benefits of adopting any regulation restricting the use of a pesticide, it is necessary to compare the risks and benefits of using that pesticide with comparable risks and benefits of alternative pesticides to which users are likely to resort. Ethion and dicofol are two important alternatives to chlorobenzilate for control of rust mites on citrus fruits (U.S. EPA 1978a). Their physical properties are compared with those of chlorobenzilate in Table 7.1. Examination of these properties and calculation of other molecular parameters indicates some common behavioral characteristics in the environment. Each has a relatively low vapor pressure, which indicates that the rate of vapor loss from sprayed surfaces may not be high. The substantial polarity of ethion indicated by its molar refraction (100.1) probably indicates a strong adsorption on surfaces. Ethion may therefore persist as a surface residue allowing dermal exposure if reentry occurs before photochemical destruction or hydrolysis. Dicofol similarly shows low vapor loss, indicating ready adsorption. As with ethion, dicofol's physical and biological properties may afford exposure. Chlorobenzilate, while also having comparatively low vapor loss, is much more susceptible to degradative chemical, biochemical, and photochemical reactions than dicofol. It should undergo metabolism more readily than dicofol and probably have less of a propensity for partitioning in lipid. Among the three compounds, ethion would probably be the least persistent and dicofol the most. In terms of biological activity, ethion is not as specific to rust mites as is chlorobenzilate, so that it is likely to have more extensive side effects than chlorobenzilate on nontarget organisms. Dicofol is specific for mites, but is not as effective for rust mites as is chlorobenzilate. This cursory examination of physical and biological properties suggests that chlorobenzilate poses less of an environmental and human hazard in terms of persistence and the possibility of undesired exposure than its substitutes, dicofol or ethion.

There are few actual data about the fate of chlorobenzilate in the environment. Several authors have studied its metabolism in plants and found that it is persistent in citrus and apple peels (Gunther *et al.* 1977, Severn 1978). When applied topically to soybean leaves, it translocates to the petioles unchanged after about 12 days (Hassan and Knowles 1969). Miyazaki *et al.* (1970) found that chlorobenzilate can be metabolized by microorganisms, particularly yeast. A study of chlorobenzilate's persistence in Florida Lakeland and Leon fine sandy soils demonstrated a half-life of 1.5–5 weeks in Leon soil and 1.5–3 weeks in Lakeland soil (Wheeler *et al.* 1973). This same study concluded that chlorobenzilate did not affect the microbiological activity in the soils. Finally, a study of environmental transport detected no chlorobenzilate in drainage water or in soil samples, following (1) the spraying of a citrus grove, (2) 39 hours of irrigation, and (3) a 2.41 cm rainfall a week later (U.S. EPA 1977).

ANALYSIS AND ASSESSMENT OF THE RISKS

The principal concern with the use of chlorobenzilate is the possibility that this chemical may increase the incidence of cancers in people exposed to it. The seriousness of this risk depends on three factors: (1)

TABLE 7.1 Physical Properties of Chlorobenzilate, Dicofol, and Ethion

Compound	Molecular Weight[a]	Solubility in Water (temperature °C)	Vapor Pressure[a] (mm Hg)	Refractive Index,[a] n_D^{20}
Chlorobenzilate	325.2	—	2.2×10^{-6} (20)	1.5727 (tech. prod.)
Dicofol	370.5	1320 μg/l (25)[b] 1.20 ppm (20)[c] 1.606 ppm (3)[c]	—	—
Ethion	384	2 ppm (22)[d] 2 ppm (?)[e]	1.5×10^{-6} (25)	1.5490 1.530 to 1.542 (tech. grade)

[a] Source: Martin (1971).

[b] Source: Weil et al. (1974).

[c] Source: F. Parveen, Environmental Health Sciences Center, Oregon State University, Corvallis, personal communication, 1975.

[d] Source: von Rumker and Horay (1972).

[e] Source: Gunther et al. (1968).

the number of people exposed, (2) the dosages to which each of them is exposed, and (3) the probable health risks from receiving these dosages. The next subsections present estimates of the extent of human exposure, followed by an assessment of that the consequences of the exposure. In a final subsection, risks posed by chlorobenzilate substitutes are evaluated and comparison compounds selected.

HUMAN EXPOSURE TO CHLOROBENZILATE

The use of chlorobenzilate on citrus fruit exposes different segments of the U.S. population to widely differing doses. The largest doses are received by citrus spray applicators and citrus fruit pickers. Much lower doses are received by people who eat foods that contain residues of the pesticide. Some of the meat consumed by residents of Florida may contain residues transmitted in the citrus pulp that is used as animal feed in the Florida livestock industry (U.S. EPA 1978a). In addition, the U.S population in general, including the residents of Florida, receives small quantitites through the ingestion of citrus fruits, some minor use crops, and products made from them. The daily doses of chlorobenzilate to these three population groups—workers, the Florida population, and the general U.S. population—are presented in Table 7.2; the derivation of these estimates and estimates of total exposure are discussed below.

TABLE 7.2 Estimated Ranges of Daily Doses of Chlorobenzilate to Three U.S. Populations Under Unrestricted Use[a]

Population (Size)	Exposure Route	Consumption (g/d)	Percent of Crop Treated	Probable-Case Assumption	Assumed Residue (ppm)		Daily Dose (μg/d)	
					Probable	Maximum-Plausible	Probable	Maximum-Plausible
Citrus ground applicators[b] (700)	Dermal						26,000	40,000
	Inhalation						1,000	
					Applicator daily total		27,000	41,000
Florida population (8×10^6)	Dietary			Accumulation Ratio				
	Beef and lamb	143.2	10	0.04	0.009	0.04	0.13	0.57
	Milk	184.7	100	0.04	0.001	0.04	0.18	7.39
	General U.S. exposure	—	—	N.A.	—	—	1.12	4.56
					Florida daily total		1.43	12.52

General U.S. population (except Florida) (212×10^6)	Dietary			Percent Residue Frequency				
	Citrus							
	Oranges	42.0	47.80	100	0.01	0.1	0.20	2.01
	Grapefruit	19.3	60.85	100	0.01	0.1	0.12	1.17
	Flavored drinks	38.0	100	100	0.02[c]	0.02[c]	0.76	0.76
	Other	12.7	31.0	100	0.01	0.1	0.039	0.40
	Other fruit							
	Apples	50.1	0.065	10	0.5	5.0	0.0016	0.16
	Pears	5.1	0.23	10	0.5	5.0	0.00059	0.059
	Nuts							
	Almonds	0.59	6.8	10	0.01	0.1	0.000040	0.0040
	Walnuts	0.59	0.46	10	0.01	0.1	0.0000027 •	0.00027
					General U.S. daily total		1.12	4.56

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[a] See text for an explanation of how estimates were derived. Citrus ground applicator estimates assume that no protective clothing is worn.

[b] Only dermal and inhalation routes of exposure are included in the applicator estimates because for this population the exposure from these routes is so much larger than from their diet that the dietary exposure is insignificant.

[c] EPA's estimate was adopted for both the probable and the maximum-plausible residue estimates since that value seemed most reasonable to the Committee, and the Committee had no basis for an alternative estimate. EPA's estimate is based on residue data for chlorobenzilate in citrus oils that are used to flavor the drinks (U.S. EPA 1979).

Occupational Exposures

Citrus Spray Applicators The Committee basically accepts OPP's estimates of the worst-case exposure situation for spray applicators. Although these estimates are methodologically sound, they are only conjecture because there are no direct observations on the dosages received by chlorobenzilate applicators. The dosage received, therefore, had to be inferred from the experience of applicators of other pesticides believed to be analogous. Under the circumstances, the Committee sees no way to improve on the estimates. The estimated probable-case doses are similarly conjectural.

A major modification of OPP's estimates, however, has to do with the number of years a worker is expected to be exposed to chlorobenzilate. The Committee will use a value of 10 years as the additional expected economic life of chlorobenzilate for use on citrus, whereas OPP assumed that chlorobenzilate would continue to be used indefinitely (see Chapter 4). If chlorobenzilate were only viable in the marketplace for an additional 10 years, the incremental exposure to citrus workers would occur only for those additional 10 years, not a full occupational lifetime.

In a study of workers exposed to various pesticides, Wolfe *et al.* (1967) measured both dermal and respiratory (i.e., inhalation) exposure under a variety of ground spray application conditions (see Table 7.3). All applications were to fruit orchards, using air-blast spray equipment. The technique for trapping residues of pesticides during application involved attaching absorbent pads to the body or clothing of the applicators to measure dermal exposure, and placing filter pads in respirators worn by the applicators to measure respiratory exposure. Trapped residues were extracted and chemical analysis of the various pesticides was carried out using a variety of analytical techniques.

Measurements of residues derived from chemical analyses indicated that exposure from spray operations was greater for the dermal route than the inhalation route (see Table 7.3). Data on dermal exposures were gathered under conditions in which applicators wore short-sleeved, open-necked shirts, with no hats or gloves (Wolfe *et al.* 1967). The investigators assumed that covered portions of the workers' bodies were completely protected. Since the data in Table 7.3 were obtained under conditions similar to those associated with the application of chlorobenzilate (i.e., similar type of crop, spray apparatus, and spray concentration), OPP assumed that they provide a reasonable basis for estimating exposure of spray applicators to chlorobenzilate (Severn 1978).

OPP's estimates of the exposure of spray applicators are based on the range of the mean values reported by Wolfe *et al.* (1967) for dermal exposures (rounded off to 15–50 mg/hour) and the maximum mean value reported for inhalation exposures (rounded off to 0.1 mg/hour) (see Table 7.3). Assuming an 8-hour workday, OPP estimated the daily dermal dose to range from 120 to 400 mg and the daily inhalation dose to be approximately 1 mg (Severn 1978).

Data upon which to base an estimate of the rate of dermal absorption of chlorobenzilate were not available either (Severn 1978). OPP therefore assumed that the chemical characteristics of chlorobenzilate are similar to those of DDT and other chlorinated hydrocarbon pesticides, and that chlorobenzilate would penetrate the skin at a rate comparable to that of DDT and other similar pesticides (Severn 1978).

Estimation of the amount of chlorobenzilate that penetrates the skin was based largely on a study by Feldmann and Maibach (1974), in which the authors studied the recovery from urine of radioactively labeled DDT, lindane, parathion, and malathion, following topical administration to the forearm in humans. They found that 5 percent of the applied dose was absorbed after the first day and that about 10.4 percent was absorbed after 5 days, although the subjects were allowed to wash the application site after the first day. The authors assumed that excretion and tissue distribution of the test compounds after dermal absorption are the same as after intravenous injection. Thus, OPP concluded that about 10 percent of the amount of chlorobenzilate that reaches the skin is absorbed (Severn 1978).

OPP estimated the *daily dose* of chlorobenzilate received by spray applicators based on the above data and assumptions. For dermal exposures without protective clothing or respirators, OPP considered 120–400 mg/day to be a reasonable estimate. Multiplying this range by a 10 percent absorption factor produced an estimate of 12–40 mg/day. OPP's daily inhalation exposure estimates assume 100 percent absorption by the lungs (Feldmann and Maibach 1974) and are estimated at 1 mg/day. Since protective clothing was not required, and climatic conditions where citrus is grown dictate against its use, OPP assumed, in the absence of other information, that spray applicators did not wear protective clothing (Severn 1978). Thus, OPP estimated that daily occupational exposure per individual for spray applicators was 12–40 mg dermally and 1 mg by inhalation, or 13–41 mg total. Because the Committee has no new data with which to make better estimates, OPP's range is retained; the lower value is assumed to be a minimum-plausible and the higher value a maximum-plausible exposure estimate. To derive a probable-case estimate, as recommended in Chapter 4, the Committee has taken the

TABLE 7.3 Dermal and Respiratory Exposure of Spray Applicators[a]

Compound	Formulation (spray) (percent)	Rate of Application (lb of active ingredient per acre)	Dermal (mg/hr)		Respiratory (mg/hr)	
			Range	Mean[b]	Range	Mean[b]
Azinphosmethyl	0.05	0.3	1.1-146	27(215)	0.02-0.08	0.04(8)
DDT	0.09	8	3.2-392	54(258)	0.02-0.27	0.1(15)
Dieldrin	0.02-0.03	2-2.5	6.3-31.1	15.5(42)	0.02-0.04	0.03(2)
Malathion	0.04-0.08	3-4	5.9-59	30(44)	0.02-0.24	0.11(7)
Parathion	0.05	2-3	1.3-38	18(40)	0.01-0.07	0.03(8)

[a] All applications were to fruit orchards, using air-blast spraying equipment.
[b] Number of samples analyzed in parentheses.

Source: Derived from Wolfe et al. (1967).

mid-point between OPP's minimum- and maximum-plausible values (assuming that the dose-response curve is linear in this range) arriving at a probable exposure estimate for applicators of 27 mg/day (see Table 7.2).

Conversion of daily occupational exposures to total incremental exposure, were chlorobenzilate to continue in use, must take into account the duration of exposure. The USDA (1977c) estimates that the current use of chlorobenzilate in ground application to citrus is carried out by as few as 714 applicators for 30–40 days/year, or by as many as 1,375 applicators for 10–20 days/year (Severn 1978). Again, OPP chose the worst-case exposure situation for an individual and assumed that the lesser number of applicators, 714, work for the greater number of days a year, 40, for approximately 40 years (U.S. EPA 1978a).

Here the Committee's estimates depart from OPP's by assuming that 10 years after a regulatory decision, chlorobenzilate will be gone from the marketplace. Instead of a 40-year exposure, then, the following calculations assume 10 additional years of ground applicator exposure at 40 days/year to approximately 700 applicators. (These values—10 years, 40 days/year, 700 applicators—are being treated as firm estimates for the sake of analytic simplicity, although in reality they should be presented as ranges.) Thus, the *total incremental lifetime exposure* of spray applicators to chlorobenzilate under assumed present conditions, i.e., no protective clothing, becomes:

Probable case = 27 mg/day × 40 days/year × 10 years = 10,800 mg.

Maximum-plausible case =
41 mg/day × 40 days/year × 10 years = 16,400 mg.

OPP also considered occupational exposure of drivers of auxiliary vehicles and helicopter pilots. We adopt OPP's conclusions that (1) since the drivers only bring their trucks to the edges of the groves and are not generally in the immediate vicinity of the sprayer, the drivers' exposure is very much less than that of the applicators (Severn 1978), and (2) spraying by helicopters (in Florida) is sporadic and is unlikely to result in significant exposure to humans because of the small amount that is applied and because the pilot is protected by the enclosed helicopter cockpit (Luttner 1977b).

The final regulatory action taken by OPP in concluding the chlorobenzilate RPAR stipulates that ground applicators have to use either protective clothing and a respirator, or a suitably equipped enclosed cab. OPP derived exposure estimates for spray applicators using protective clothing and respirators. OPP's estimate of the reduction in dermal exposure afforded by protective clothing (coveralls, a cloth cap, and gloves) was based on the assumption that covered skin areas are completely protected. According to Hayes (1975), the body surface areas of hands, arms, face, and neck make up approximately 16 percent of total body surface area. If all these areas except the face are covered, the remaining exposed surface would be 3.5 percent of total body surface, resulting in a reduction of dermal exposure by a factor of approximately 4.5 (Severn 1978).

Using this factor of 4.5, OPP derived a dermal exposure of 3–9 mg/day (12–40 mg/day ÷ 4.5) with protective clothing. OPP also concluded that respirators would effectively eliminate exposure by inhalation (estimated at 1 mg/day) and further reduce dermal exposure to the face by 1–3 mg/day. Thus, for applicators wearing both protective clothing and respirators, daily exposure could be reduced to between 2 and 6 mg/day, minimum-plausible and maximum-plausible exposure, respectively (U.S. EPA 1979). Total incremental lifetime exposure of an applicator in full compliance with the new chlorobenzilate regulations—that is, with protective clothing and respirators—would be:

$$\text{Probable case} = 4\ \text{mg/day} \times 40\ \text{days/year} \times 10\ \text{years} = 1{,}600\ \text{mg.}$$

$$\text{Maximum-plausible case} = 6\ \text{mg/day} \times 40\ \text{days/year} \times 10\ \text{years} = 2{,}400\ \text{mg.}$$

However, these estimates of the effects of the regulation cannot be confirmed until the required applicator exposure data are submitted and evaluated. In fact, when calculating risk to citrus spray applicators associated with the regulatory option that requires protective clothing and respirators, the Committee assumes only 50 percent compliance as the probable case and 20 percent in the maximum-plausible exposure case. These assumptions are based on the difficulty of enforcement and the Committee's direct experience with citrus growers and researchers in Texas, which indicated a disbelief that chlorobenzilate is hazardous.

One of the major uncertainties in the forgoing analysis is the validity of the dermal absorption rate (i.e., 10 percent). Chlorobenzilate is relatively polar compared to other compounds of its general type, such as DDT, so that its relative dermal uptake should be less than that for DDT. Reliance on the general data developed by Wolfe *et al.* (1967) for estimating inhalation and dermal exposures is unfortunate, partly because so few compounds were tested but, more importantly, because the absorbent pads used in their tests (cotton gauze pads) lack all the significant characteristics of human skin. The result of these considerations is that errors of several orders of magnitude might be involved in these estimates and passed on to the estimated inhalation exposure calculated by the average dermal to inhalation ratios reported by Wolfe *et al.*

Research on these topics would allow for better estimates through development of appropriate physicochemical correlates to relative dermal absorption of those pesticides already investigated. However, the data upon which the forgoing analysis relies for its estimates of dermal absorption of chlorobenzilate (i.e., Feldmann and Maibach 1974) are not helpful, as the correlation between the data and actual physicochemical activities appears small or non-existent. Consequently, use of an average dermal absorption rate for chlorobenzilate is necessary and unavoidable, though weak.

Fruit Pickers The Florida citrus crop is harvested from about November to May, using mostly migrant workers (Severn 1978). Data cited by the Federal Working Group on Pest Management (1974) show that in January 1971, 25,431 migrant and contract workers were employed in Florida, whereas in July of that year only about 450 were employed. During harvesting season, as many as 25,000–30,000 citrus pickers may be occupationally exposed to chlorobenzilate (U.S. EPA 1978a).

OPP's analysis of the risks associated with the use of chlorobenzilate, however, does not evaluate the extent of exposure of citrus pickers during harvesting activities. The Committee agrees that lack of data on (1) the extent of dislodgeable residues on citrus fruit and foliage, and (2) the extent of transfer of these residues to citrus pickers, either by dermal or vaporization routes, precludes quantitative assessment of exposure for this particular group (Severn 1978).

Since exposure of citrus pickers occurs after chlorobenzilate has been applied, OPP assumed that their exposure is less than that of spray applicators (U.S. EPA 1978a). However, chlorobenzilate residues on citrus fruit and foliage may be a primary source of contact (i.e., dermal) exposure. Residue data, together with factors indicating the degree of absorption by the skin and duration of exposure, would allow for estimation of exposure of citrus fruit pickers. The regulatory action taken for chlorobenzilate calls for monitoring studies of the levels of chlorobenzilate residues at harvest time and of the actual dermal doses that the workers receive (U.S. EPA 1978a).

Dietary Exposures

As noted in Chapter 4, the Committee endorses the general procedure used by OPP to estimate dietary exposures. The general equation OPP uses to determine daily doses is: consumption (g/day) × extent of pesticide use on crop (percent) × maximum residue (ppm) = maximum ingestion (μg/day). The Committee will, however, derive probable levels of exposure in addition to the worst-case (maximum-plausible) situation to which OPP's estimates are limited. Also, the Committee dissents from some of the detailed procedures used by OPP: in particular, those for determining assumed residue levels and the assumption that populations will receive chlorobenzilate through their diet for an entire 70-year lifetime. The estimates used by the Committee are derived in the following two subsections.

Florida Population The population of Florida is assumed to undergo unique exposure to chlorobenzilate due to the use of treated citrus pulp in livestock feed. Chlorobenzilate residues are assumed to be ingested by Floridians via the meat and meat by-products of Florida beef and lamb, and via milk from the cattle.

The procedure recommended and used by the Committee to estimate probable exposure involves using an observed residue accumulation ratio to estimate chlorobenzilate residue levels in beef, lamb, and milk, instead of analytical sensitivity levels. The advantage of this procedure is that it is pharmacodynamically sound, whereas the maximum-plausible residue estimates are not. The critical assumption in this procedure is that the accumulation ratio is constant over a wide range of dosage rates.

An accumulation ratio for chlorobenzilate in cattle fat can be derived using data from a study by Mattson and Insler (1966). Mattson and Insler studied levels of chlorobenzilate residues in cattle and sheep that had been fed a daily ration containing chlorobenzilate over a period of 28 days. Following analysis of several different tissues, residues of chlorobenzilate were found only in cattle fat at the highest feeding level, 340 mg/animal/day. Assuming that a cow eats approximately 20 kg of feed a day, the feed resulting in ingestion of 340 mg/animal/day would contain chlorobenzilate at a concentration of 17 ppm. The average residue level for three fat samples was 0.63 ppm. The observed accumulation ratio, therefore, is ppm in fat ÷ ppm in feed, or $0.63 \div 17 = 0.037 \cong 0.04$. No residues were detected at an analytical limit of 0.3 ppm when the feeding level was 110 mg/animal/day. However, the probable residue in fat calculated by estimating from the accumulation ratio would be 0.22 ppm (a feeding level of 110 mg/day ÷ 20 kg consumed = 5.5 ppm of chlorobenzilate in the diet; 5.5 ppm × 0.04 accumulation ratio in fat = 0.22 ppm residue in fat).

Adopting OPP's estimate of 2 ppm as a reasonable upper limit of residue in citrus pulp (based on maximum measured residues in Florida citrus pulp, FY 1976 data; Severn 1978), the Committee estimates that the steady-state residue of chlorobenzilate in animal fat from using treated citrus pulp in livestock feed is the accumulation ratio (0.04) × the concentration of chlorobenzilate in the diet (2.0 ppm in pulp × 16 lb of pulp ÷ 20 kg diet), or 0.04 × 0.73 ppm = 0.029 ppm. Beef cuts averaging 30 percent fat (a maximum value) would then contain 0.009 ppm residual chlorobenzilate. If Florida beef and lamb were consumed at a rate of 143.2 g/day (Schmitt 1977, based on USDA 1972), the probable estimate of ingestion of chlorobenzilate would be 1.29 μg/day (based on all animals being fed pulp under the above conditions). However, we adopt OPP's estimate that only 10 percent of the animals are fed citrus pulp, reducing the probable ingestion estimate to 0.13 μg/day (see Table 7.2).

The method used by OPP, and adopted by the Committee, to derive maximum-plausible estimates of daily chlorobenzilate ingestion from beef and lamb is based on the detection level of chlorobenzilate in fat. This method may overestimate exposure by relying on maximum analytical sensitivity. In OPP's chlorobenzilate estimates, the key assumption fits the analytical detection limit to an experimental dosing rate that was observed not to produce residues exceeding that detection limit. Thus, the resulting estimate could be pharmacodynamically unsound. However, with chlorobenzilate this approach actually matched the pharmacodynamic estimate quite closely; 110 mg/day ingestion yielded an assumed 0.3 ppm concentration in fat (OPP) rather than 0.22 ppm as estimated in this report.

The maximum practical amount of citrus pulp in animal feed is 16 lb/day/animal (Severn 1978). The amount of chlorobenzilate ingested by an animal fed 16 lb/day of dried citrus pulp is 16 lb/day × 454 g/lb × 2 ppm residue in feed, or 15 mg/day. Using the 0.3 ppm detection level in fat as the maximum fat and meat residue to be expected from feeding 110 mg/animal/day of chlorobenzilate (Mattson and Insler 1966), by extrapolation OPP calculates the maximum residue level expected from feeding 15 mg/day as 0.3 ppm × (15 mg ÷ 110 mg), or 0.04 ppm. Multiplying this assumed residue by daily meat consumption and percent of animals receiving treated feed gives a maximum-plausible daily human ingestion estimate of 0.04 ppm × 143.2 g/day × 10% = 0.57 μg/day (see Table 7.2).

To determine incremental lifetime doses for the Florida population, the daily doses are multiplied by the assumed duration of exposure, discounting past exposures. Using the assumption that chlorobenzilate will remain on the market for an additional 10 years if reregistered (see Chapter 4), the additional lifetime doses to Floridians from chlorobenzilate in beef and lamb are:

Probable case (beef, lamb) =

0.13 μg/day × 365 days/year × 10 years = 475 μg.

Maximum-plausible case (beef, lamb) =

0.57 μg/day × 365 days/year × 10 years = 2,081 μg.

The accuracy and validity of the accumulation ratio procedure for estimating the daily dose of chlorobenzilate to the Florida population depend on the following assumptions:

1. That neither cumulative dosing, nor dosing at different rates, alters the metabolism of the chemical. Studies have shown the accumulation ratio to be linear over a 100- to 1,000-fold concentration range in several published studies of chemicals similar to chlorobenzilate (e.g., Quaife *et al.* 1967, Walker *et al.* 1969).
2. That steady-state equilibrium is assumed, thus continuous dosing to the time required for equilibrium is necessary.
3. That external modifiers affecting metabolism, distribution, and elimination of the chemical are constant.

Most of these conditions also pertain to the worst-case (maximum-plausible estimate) procedure, although these latter estimates also include the analytical threshold as a major uncertainty. As noted earlier, if the accumulation ratio method were used in the case of chlorobenzilate, the maximum dosing rate not producing an analytically significant residue (i.e., 110 mg/day in beef cattle) would be predicted to produce a 0.22 ppm residue in fat, rather than OPP's 0.3 ppm (minimum-sensitivity) value; this close agreement indicates the innocuousness of the analytical sensitivity approach in this instance, but OPP cannot expect such coincidence in general.

Residues in milk are concentrated in milk fat and are essentially in equilibrium with body fat at concentrations similar to those in body fat. Therefore, probable estimates of residue concentrations in milk may be derived from the accumulation ratio approach described for beef. With chlorobenzilate residues in pulp at a level of 2 ppm, the resulting residue level in milk fat would be approximately 0.029 ppm (0.73 ppm in feed × the accumulation ratio, 0.04). This establishes a residue estimate of 0.001 ppm for milk containing 3.5 percent fat (3.5% × 0.029 ppm). If 184.7 g of milk were consumed daily and all of it contained residues (adopting OPP's data, Schmitt 1977 based on USDA 1972), the probable-case estimate of chlorobenzilate ingestion for Floridians would be 0.18 μg/day (see Table 7.2). This value is probably high, since animals that secrete milk eliminate a significant amount of daily fat and thus eliminate residual chlorobenzilate faster than in nonlactating animals; the result is in an overall lowering of the steady-state equilibrium level.

OPP's maximum-plausible estimates of chlorobenzilate ingestion by Floridians via milk were derived from limited data based on analytical sensitivity indicating that cattle consumption of treated feed may result in chlorobenzilate residues in milk from 0.0024 to 0.04 ppm (U.S. EPA 1978a). The Committee used the higher value of this residue range, 0.04, to derive a single maximum-plausible exposure estimate of 7.39 μg/day (184.7 g/day × 0.04 ppm; see Table 7.2).

Again, incremental lifetime doses are calculated by multiplying the daily rate by 10 years:

Probable case (milk) = 0.18 μg/day × 365 days/year × 10 years = 657 μg.

Maximum-plausible case (milk) =

7.39 μg/day × 365 days/year × 10 years = 26,974 μg.

General U.S. Population The Committee has prepared estimates of probable daily doses received by the general U.S. population through the diet and has adopted OPP's worst-case or maximum-plausible estimates. These estimates are presented in Table 7.2, and their derivation is sketched below. To convert these to lifetime exposures, one would

TABLE 7.4 Florida State Monitoring Data for Chlorobenzilate Residues in Fresh Citrus Fruit

Season	Percent of Samples with Positive Concentrations	Tolerance (ppm)	Average Residue (ppm)	Range of Residues (ppm)
1974-1975	35	5	0.42	0.05-1.82
1975-1976	35	5	0.36	0.07-1.06
1976-1977	38	5	0.040	0.06-1.73

Source: Dennis (1977).

multiply by the expected additional 10-year market life of chlorobenzilate discussed earlier.

The Committee's estimates of probable levels of daily chlorobenzilate ingestion from citrus fruits and products are 10 percent of the maximum-plausible estimates, except for flavored drinks (see Table 7.2). Both the probable and maximum-plausible estimates rely on OPP's average consumption figures, taken from USDA surveys (Schmitt 1977, based on USDA 1972) and OPP's estimate of the percentage of the crop treated with chlorobenzilate (U.S. EPA 1978a). Both estimates also use the analytical sensitivity limit as the assumed residue level (except in the case of flavored drinks where residue data are used); however, the maximum-plausible estimates assume an analytical sensitivity of 0.1 ppm, whereas the probable case uses the sensitivity of new analytical methods, 0.01 ppm.

Justification for the use of analytical detection limits comes from a review of actual residue data. Data on chlorobenzilate residues were provided by the Florida Department of Agricultural and Consumer Services (Dennis 1977) and the FDA (Severn 1978), and are presented in Tables 7.4 and 7.5, respectively. Both surveys indicate that residues of chlorobenzilate are well below the established tolerances in the samples tested. Thomas (1976) also carried out a limited monitoring study of chlorobenzilate residues in fresh, canned, and frozen citrus produce obtained in the Washington, D.C. area; residues above 0.1 ppm were found in 7 of 79 samples, all of which were fresh whole citrus.

All of the citrus residue data were derived from analyses of whole citrus fruit. It is likely, however, that the residues originated principally from the peels, since detection of significant amounts of chlorobenzilate in the edible portion has not been reported (see, for example, Bartsch *et* *al.* 1971). Even during juice-making procedures, transfer of chlorobenzilate from the oil-rich peel to the expressed juice is minimal. According to Kesterson *et al.* (1971), there exists a misconception that oil is pressed from the peel or fruit during the extraction of citrus oil. They note rather that oil cells are ruptured by pressure or abrasion, and the oil washed away. Here, the partitioning behavior of chlorobenzilate between aqueous and oil phases would prevent even miminal residues in juice.

Gunther (1969) presented experimental data showing that chlorobenzilate residues were undetectable in juice under conditions where the detection limit was 1/100 the residue concentration in lemon rind (20 ppm). Even after considering that the laboratory preparation of juice might be "cleaner" than commercial juicing operations, it remains unlikely that chlorobenzilate residues in juice would regularly approach 0.1 ppm concentration when the whole fruit residues established in the monitoring surveys were only 0.1–0.5 ppm, with these being detected in no more than 10 percent of the samples (see Table 7.5). Whole juice monitoring has not produced detectable chlorobenzilate.

Since the majority of citrus products consumed as food comes from the pulp and not the peel, it is assumed that chlorobenzilate residues ingested from consumption of citrus would not be detectable by current monitoring techniques. However, since residues can be present up to the limit of analytical sensitivity and still be undetectable, the complete absence of chlorobenzilate in citrus food products cannot be demonstrated.

For maximum-plausible residual estimates, OPP concluded that the Bartsch *et al.* (1971) survey provided the best available data on chlorobenzilate residues in citrus. These workers found residues in pulp to be less than 0.1 ppm, using gas chromatography with a detection limit of 0.1 ppm. OPP therefore assumed that 0.1 ppm was a reasonable upper limit of actual chlorobenzilate residue levels that would pass undetected in edible portions of citrus (Severn 1978).

For the probable-case estimates, the Committee assumes that since new analytical methods are sensitive to 0.01 ppm, and the residue is virtually all in the peel, residues in the edible portion of citrus might be present up to a limit of 0.01 ppm. Estimation of the amount of chlorobenzilate in flavored fruit drinks was based on OPP's residue data for chlorobenzilate in citrus oils, which are used to flavor the drinks (U.S. EPA 1979). OPP's estimate was adopted for both the probable and maximum-plausible residues since that value seemed reasonable to the Committee, and the Committee had no basis for an alternative estimate. Probable and maximum-plausible estimates of chlorobenzilate ingestion

TABLE 7.5 U.S. Food and Drug Administration Data for Chlorobenzilate Residues in Raw Agricultural Commodities

Year	Commodity	Tolerance (ppm)	Number of Samples with Positive Concentrations	Range of Positive Concentrations (ppm)
FY 1974	Large fruits	5	5 of 481	trace-0.03
FY 1976	Large fruits	5	5 of 511	0.04-1.00
FY 1976	Vine and ear vegetables	?	2 of 680	0.04-0.10
FY 1976	Silage	?	2 of 111	0.51-1.50
FY 1976	Processed animal food and fruit by-products	?	9 of 31	0.11-2.01[a]

Individual Commodity Samples with Chlorobenzilate Residues

Year	Commodity	Tolerance (ppm)	Number of Samples	Range (ppm)
FY 1976	Oranges (Florida)	5	6	0.08-0.83
FY 1976	Animal feed (Florida, citrus pulp)	?	11	0.39-2.02
FY 1976	Tomatoes (Tennessee)	?	2	0.07-0.08

[a] One sample had more than 2.01 ppm.

Source: Severn (1978).

via citrus are shown in Table 7.2 and are calculated using OPP's general equation: consumption × extent of use on crop × residue = ingestion.

Because of a lack of data on residues in apples and pears, OPP used the 5.0 ppm tolerance value as a basis for estimating maximum-plausible doses. No large fruit sample analyzed, however, contained more than 1.0 ppm residual chlorobenzilate and only 1 percent of the samples analyzed had any detectable residue even though all the fruit had been treated (Table 7.5). Therefore, not only is the tolerance level an excessive estimate for the concentration in whole fruit, but it also ignores the fact that these fruits are not primarily consumed whole, as assumed, but in several processed forms (e.g., washed, peeled, or cooked).

The probable-case estimate, therefore, assumes that only 10 percent of the treated crop contains residues (i.e., residue frequency = 10 percent), and uses the average reported residue (0.50 ppm) to obtain a responsibly conservative—on the side of maximizing risk—value. For apples and pears, ingestion estimates are (see Table 7.2):

Probable case (apples) =

50.1 g/day × 0.065 (% crop treated) × 0.5 ppm residue × 10% residue frequency = 0.0016 μg/day.

Maximum-plausible case (apples) =

50.1 g/day × 0.065 (% crop treated) × 5 ppm residue = 0.16 μg/day.

Probable case (pears) =

5.1 g/day × 0.23 (% crop treated) × 0.5 ppm residue × 10% residue frequency = 0.0006 μg/day.

Maximum-plausible case (pears) =

5.1 g/day × 0.23 (% crop treated) × 5 ppm residue = 0.06 μg/day.

Calculations for chlorobenzilate ingestion via nuts are based on analytical detection limits and, for the probable case, a 10 percent residue frequency:

Probable case (almonds) =

0.59 g/day × 6.8 (% crop treated) × 0.01 ppm residue × 10% residue frequency = 0.00004 μg/day.

Maximum-plausible case (almonds) =

0.59 g/day × 6.8 (% crop treated) × 0.1 ppm residue
= 0.004 μg/day.

Probable case (walnuts) =

0.59 g/day × 0.46 (% crop treated) × 0.01 ppm residue
× 10% residue frequency = 0.000003 μg/day.

Maximum-plausible case (walnuts) =

0.59 μg/day × 0.46 (% crop treated) × 0.1 ppm residue
= 0.0003 μg/day.

The sum total of daily doses of chlorobenzilate received by the general U.S. population in the diet, shown in Table 7.2, ranges from 1.12 to 4.56 μg/day, or 4,088 to 16,644 μg/lifetime total, assuming chlorobenzilate is present for 10 more years.

PATHOLOGICAL ACTIVITY OF CHLOROBENZILATE

On May 26, 1976, OPP issued an RPAR for chlorobenzilate based on oncogenic effects (U.S. EPA 1976b). Although the studies on which the RPAR was based included data indicating that chlorobenzilate has adverse effects on the testes of rats, OPP's RPAR notice neither mentioned the issue of testicular atrophy nor invited registrants to comment on this issue in their rebuttals. Concern for this potential adverse effect was not raised until the later stages of the chlorobenzilate RPAR proceeding, and then OPP concluded that the data were insufficient to establish the biological significance of adverse testicular effects. Thus, oncogenic effects were the main issue in the chlorobenzilate RPAR proceedings. The following assessment of the pathological activity of chlorobenzilate is restricted to oncogenic effects.

OPP's decision to issue an RPAR against chlorobenzilate was based on two studies in which tumors developed in rats (Horn *et al.* 1955, Woodard Research Corporation 1966) and one study in which tumors developed in mice (Innes *et al.* 1969). Subsequently, NCI submitted additional chlorobenzilate carcinogenesis bioassay data on both rats and mice. OPP's final risk estimates were based on the Innes *et al.* (1969) study, which showed that chlorobenzilate produced statistically significant increases in the incidence of tumors in male mice (U.S. EPA 1979).

After additional review and validation procedures, OPP determined that the Horn *et al.* (1955) and Woodard Research Corporation (1966) studies were unreliable. Upon further consideration, the EPA's CAG chose to base the chlorobenzilate risk estimates on the Innes rather than the NCI study because the oncogenic response per unit of dose of chlorobenzilate in the Innes study was 5 times greater (U.S. EPA 1978a). Also, animals in the Innes study were fed the compound beginning at a younger, more susceptible age. Thus, the CAG concluded that the Innes data were more appropriate for risk calculations under the conservative assumption that human response is similar to the most sensitive animal species and because of the possibility that people will be exposed to chlorobenzilate as infants (U.S. EPA 1978a).

The Committee's estimate of the carcinogenicity of chlorobenzilate is detailed in Appendix C. The Committee endorses OPP's decision to use the Innes data as a starting point and based its own calculations on those data (see Appendix C), using the procedure recommended in Chapter 4.

The CAI calculated for chlorobenzilate from the Innes data lies in the range 0.15–0.38 (using a 90 percent confidence interval) with a most-probable estimate of 0.27. The use of data from the laboratory experiment that showed the highest incidence of tumors, disregarding several other experiments that also were available, naturally imparts a bias toward a worst-case estimate. Because the relationship between tumor incidence in laboratory animals and cancer incidence in humans is so obscure, the Committee elected to follow the policy of the CAG in this regard. This bias, however, should be kept in mind in interpreting the following analysis.

ESTIMATION OF RISK UNDER VARIOUS REGULATORY OPTIONS

By risk we mean the combined effect of the number of people exposed to pathogenic compounds, the levels of dosage received by those people, and the pathological activity of the compounds. All three components of risk have been discussed, and it remains to put them together.

Separate estimates of risk are required for each regulatory option considered, so that they can be compared. The Committee evaluated the risks of the following five options, which it believes to be the salient ones (see the final major section of this chapter for a discussion of why these options are chosen):

A. Continue registration of all uses.
B. Cancel all noncitrus uses.
C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions of registration to require protective clothing and respirators; cancel all other uses.
D. Cancel chlorobenzilate use on citrus to take effect after 5 years, and in the interim apply Option C.
E. Cancel all uses.

The first step in estimating the risks associated with an option is to estimate the lifetime doses of chlorobenzilate to which members of different population groups will be exposed if that option is adopted. This step is the subject of the next subsection. But one consequence of any option other than the status quo may be to increase the use of alternative pesticides (see Chapter 6), some of which may be carcinogenic (or otherwise hazardous). Thus, the second step is to estimate the doses of those alternative pesticides to which members of the population will be exposed if chlorobenzilate is regulated in accordance with that option. This step will be taken in the second subsection. These two estimates must then be combined to determine the "equivalent chlorobenzilate lifetime exposure" for each population. This combining, however, is not one of simple addition; the doses of chlorobenzilate and each of its alternatives have to be weighted in proportion to their CAI's (or other appropriate pathogenic activity indicator) before being summed (see Chapter 4). This step is taken in the third subsection. Finally, a conception of the virulence of chlorobenzilate must be introduced. This is accomplished by comparing the experimentally observed CAI for chlorobenzilate to those of appropriate reference compounds. In this way the relative virulence of chlorobenzilate becomes known. This step is taken in the last subsection before the economic evaluation of benefits is undertaken.

Lifetime Doses of Chlorobenzilate

Both the length of exposure to chlorobenzilate and the intensity will vary with the various regulatory options. Exposure will be of maximum duration and dosage for all populations for Option A. For Option B, exposure to the Florida and general U.S. populations will be reduced by the noncitrus contribution. As it happens, the doses received by ingestion of noncitrus products are too small to affect the numerical estimates (which are truncated after two or three significant figures) that will be derived below except in the maximum-plausible cases. Option C differs from Option B in that the dosage received by citrus ground applicators is also reduced. For Option C, 50 percent compliance with the protective clothing and respirator requirements is assumed as the probable case and 20 percent as the maximum-plausible exposure case, as explained earlier (see this chapter, section on Human Exposure to Chlorobenzilate). This assumption affects the estimated lifetime exposure values. For Option D, citrus exposures will continue for only 5 additional years, noncitrus exposures will be eliminated immediately, and the ground applicator exposures during the 5-year period will be reduced as in Option C. For Option E, there will of course be no chlorobenzilate exposure.

The resulting estimates of exposure to chlorobenzilate under the five options are presented in Table 7.6. The first column displays the daily doses, in millimoles per kilogram of body weight, that the Committee estimates to be most probable for members of three population groups under each of the five options. These figures are derived from the estimated daily doses in micrograms, whose calculation was described in the preceding section, by dividing them by the gram molecular weight of chlorobenzilate (325.2) and by the average weight of an adult man (70 kg). For example, the probable daily dose received by a ground applicator under Options A or B was computed by:

$$\frac{27{,}000\ \mu\text{g/day}}{325.2\ \text{g/mole} \times 70\ \text{kg}} = 12 \times 10^{-4}\ \text{m mole/kg.}$$

The second column is similar except that it records the maximum daily doses that the Committee judges to be at all possible. In view of the many inadequacies of the data and the uncertainties that have been discussed above, this judgment is necessarily subjective. In each case where such judgments had to be made, the Committee endeavored to arrive at a figure that corresponded to the upper limit of a formal 90 percent confidence interval, that is, a figure that we felt would be exceeded by actual results if the option were adopted in about 5 percent of the cases in which such judgments were made. All the estimates of maximum-plausible exposure in this analysis are to be interpreted in that sense.

The third column computes the average number of days of exposure of members of the population to the estimated dosages. The genesis of these estimates has already been described. The figures shown are most-probable estimates; in fact, the remaining economic life of chlorobenzilate may turn out to be greater or less than 10 years, and the average number of days that an applicator is exposed may differ from the 40 days a year that we believe most likely. In the interest of simplicity, no attempt was made to define a range of estimating errors. We believe that

TABLE 7.6 Lifetime Dose per Individual of Chlorobenzilate[a] by Regulatory Option

Regulatory Option[b]	Daily Dose (m moles/kg)[c] Probable	Daily Dose (m moles/kg)[c] Maximum-Plausible	Duration	Lifetime Dose (m moles/kg)[d] Probable	Lifetime Dose (m moles/kg)[d] Maximum-Plausible
Citrus Ground Applicators (700)					
A	0.0012	0.0018	40 d/yr × 10 yr	0.48	0.72
B	0.0012	0.0018	40 d/yr × 10 yr	0.48	0.72
C[e]	0.00068	0.0015	40 d/yr × 10 yr	0.27	0.60
D[e]	0.00068	0.0015	40 d/yr × 5 yr	0.14	0.30
E	0	0	0	0	0
Florida Population (8×10^6)					
A	0.062×10^{-6}	0.55×10^{-6}	365 d/yr × 10 yr	0.23×10^{-3}	2.01×10^{-3}
B[f]	0.062×10^{-6}	0.54×10^{-6}	365 d/yr × 10 yr	0.23×10^{-3}	1.97×10^{-3}
C[f]	0.062×10^{-6}	0.54×10^{-6}	365 d/yr × 10 yr	0.23×10^{-3}	1.97×10^{-3}
D[f]	0.062×10^{-6}	0.54×10^{-6}	365 d/yr × 5 yr	0.11×10^{-3}	0.99×10^{-3}
E	0	0	0	0	0

General U.S. Population (except Florida) (212 × 10⁶)

A	0.049×10^{-6}	0.20×10^{-6}	365 d/yr × 10 yr	0.18×10^{-3}	0.73×10^{-3}
B[f]	0.049×10^{-6}	0.19×10^{-6}	365 d/yr × 10 yr	0.18×10^{-3}	0.69×10^{-3}
C[f]	0.049×10^{-6}	0.19×10^{-6}	365 d/yr × 10 yr	0.18×10^{-3}	0.69×10^{-3}
D[f]	0.049×10^{-6}	0.19×10^{-6}	365 d/yr × 5 yr	0.089×10^{-3}	0.35×10^{-3}
E	0	0	0	0	0

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[a] These values are for chlorobenzilate exposure only; exposures from chlorobenzilate substitutes are not included. Total exposures from chlorobenzilate and its substitutes are shown in Table 7.28.

[b] Regulatory options:

A. Continue registration of all uses.
B. Cancel all noncitrus uses.
C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions of registration to require protective clothing and respirators; cancel all other uses.
D. Cancel chlorobenzilate use on citrus to take effect after 5 years, and in the interim apply Option C.
E. Cancel all uses.

[c] Probable- and maximum-plausible-case estimates are derived from Table 7.2 and the text.

[d] Lifetime dose equals daily dose times duration.

[e] These options assume that 50 percent compliance with the clothing and respirator restrictions is probable and 20 percent compliance would be the worst case. To derive daily dose estimates, then, for the probable case it is assumed that 50 percent of the population receive the probable dose with protective clothing and respirators, 4 mg/d, and 50 percent receive the probable dose without protective clothing and respirators, 27 mg/d, for a combined value of 15.5 mg/d.

Similarly, for the worst-case compliance, 20 percent would receive daily doses of 6 mg and 80 percent 41 mg, for a combined value of 34 mg/d.

[f] Exposure for these options is reduced by the daily dose of chlorobenzilate received via noncitrus food commodities. This reduction is so small, however, that it only shows up in the maximum-plausible daily dose estimates.

if the attempt were made, it would not substantially affect evaluations of the regulatory alternatives. The final two columns are estimates of lifetime doses, obtained by multiplying either the first or second columns by the third one.

Risks from Alternative Pesticides

The considerations discussed in Chapter 3 determine how much information about and assessment of the alternatives to chlorobenzilate use on citrus are necessary (see Chapter 3, section on Modification to the Preliminary Ranking: The Role of Alternative Pesticides). For example, if it were assumed that no Class A (i.e., apparently a potential toxic hazard) or B (i.e., insufficient data to permit a reasonable judgment) substitutes continue to be available, and the RPAR evaluation of chlorobenzilate alone showed risks to exceed benefits, then no consideration of alternatives would be necessary; chlorobenzilate use on citrus should be severely restricted or cancelled.

In fact, however, if chlorobenzilate were the only miticide registered for use on citrus, its withdrawal would result in a significant deterioration in the cosmetic quality of the fruit (especially on Florida and Texas citrus). In addition, some have argued that the failure to treat for rust mites could lead to significant losses in yield per acre (see Luttner 1977b). It is conceivable that benefits of chlorobenzilate use would outweigh risks if no other miticides were available. Consequently, it is necessary to investigate benefits and risks of chlorobenzilate use under the assumption that some or all of the currently registered alternatives will remain available.

OPP has identified at least seven apparently viable alternatives to chlorobenzilate for use on citrus: fenbutatin-oxide, dicofol, ethion, sulfur, oil, propargite, and carbophenothion. Because pesticide formulations have not yet been classified into Classes A, B, and C, as recommended in Chapter 3, it is unclear to which class each chlorobenzilate substitute belongs. On the basis of preliminary toxicity profiles prepared by HED, concern might be raised about each of the substitutes for reasons of either acute or chronic toxicity (Burnam 1977, Bushong 1977). In particular, ethion and carbophenothion appear to have high acute toxicities, and dicofol has been shown to be carcinogenic in an NCI rodent bioassay study (NCI 1978). For the following discussion, then, it is prudent to assume that all of the substitutes would be either Class A or Class B compounds.

If it is assumed that all of the substitutes will remain available, the benefit-risk estimates for chlorobenzilate should be calculated taking into account risks and benefits of the substitutes if chlorobenzilate were regulated. (OPP has done this in a rough, largely qualitative fashion in PD's 3 and 4.) If this assessment clearly shows that benefits of continuing to use chlorobenzilate exceed risks, then it should be reregistered for citrus. If this is not clear, however, it then becomes important to identify the substitute pesticide or pesticides causing the ambiguity and to conduct a "qualified" RPAR on it or them (see Chapter 3).

To illustrate how alternatives would be taken into consideration using the risk assessment procedures recommended in Chapter 4, the Committee has chosen dicofol. This selection is based on OPP's information that, from NCI animal bioassay data, dicofol is about 12 times more potent as a carcinogen than chlorobenzilate (U.S. EPA 1978a). Thus, an assessment of the risks from increased use of dicofol if chlorobenzilate were to be cancelled appears crucial to making a sound decision on chlorobenzilate. The following discussion is divided into two subsections addressing, first, exposure, then pathological activity.

Dicofol Exposure Estimates of the additional daily dose of dicofol to each exposed population if chlorobenzilate were to be cancelled are presented in Table 7.7. Their derivation is sketched below. Estimates of total lifetime incremental exposure to dicofol for the various regulatory options are then presented in Table 7.8.

To calculate the increased exposure to dicofol if chlorobenzilate were cancelled (regulatory Option E) or restricted (Options B to D), it is necessary to have an estimate of the extent to which dicofol will replace chlorobenzilate in citrus and noncitrus uses. From the benefit analysis in the next major section of this chapter, the Committee estimates that dicofol will replace from 13,500 to 67,500 chlorobenzilate acre-treatments, or 2–10 percent of the total citrus use.[1] For simplicity, the Committee assumed that the replacement rate for dicofol on noncitrus (other fruits and nuts) would be the same as for citrus.

For applicators it was assumed that daily dicofol exposure would be the same as for chlorobenzilate multiplied by the 2.4 times greater application rate (Bushong 1977) of dicofol's active ingredient. Implicit in this assumption is the expectation that the mode of application and subsequent behavior of dicofol, including metabolism, will be similar to that of chlorobenzilate. The basis for these assumptions has not been explored, and better exposure estimates might be calculable; but the ones used here will suffice for the sake of illustration. Estimates of the incremental daily doses of dicofol from dermal and inhalation routes are shown in Table 7.7.

To take account of the fact that under Options D and E when

TABLE 7.7 Estimated Ranges of Additional Daily Doses of Dicofol Resulting from Chlorobenzilate Cancellation[a]

Population (Size)	Exposure Route	Consumption[b] (g/d)	Percent of Crop Treated[c]	Assumed Residue (ppm)		Daily Dose[f] (μg/d)	
				Probable[d]	Maximum-Plausible[e]	Probable	Maximum-Plausible
Citrus ground applicators[g] (700 exposed 2-10 percent of the days they would have been exposed to chlorobenzilate)	Dermal					62,400	96,000
	Inhalation					2,400	
				Applicator daily total		64,800	98,400
Florida population (8×10^6)	Dietary						
	Beef and lamb	143.2	0.2-1.0	0.36	0.36	0.10	0.52
	Milk	184.7	2-10	0.046	0.046	0.16	0.78
	General U.S. exposure					0.11	2.29
				Florida daily total		0.37	3.59

General U.S. population (except Florida) (212×10^6)	Dietary						
	Citrus						
	Oranges	42.0	0.95-4.78	0.05	0.5	0.020	0.5
	Grapefruit	19.3	1.2-6.08	0.05	0.5	0.012	0.29
	Flavored drinks	38.0	2-10	0.1[h]	0.01[h]	0.076	0.38
	Other	12.7	0.62-3.1	0.05	0.5	0.0039	0.1
	Other fruit						
	Apples	50.1	0.0013-0.0065	2.5	25.0	0.0016	0.04
	Pears	5.1	0.0046-0.023	2.5	25.0	0.00059	0.015
	Nuts						
	Almonds	0.59	0.14-0.68	0.05	0.5	0.000041	0.001
	Walnuts	0.59	0.009-0.046	0.05	0.5	0.0000027	0.00007
				General U.S. daily total		0.11	1.34

---

[a] Where daily dose estimates involve combining variables that are reported as ranges, the procedures described in Appendix F are used.

[b] Same as for commodities containing chlorobenzilate. It is assumed that dicofol is a viable substitute on all crops on which chlorobenzilate is currently used.

[c] Calculated by multiplying the percent of chlorobenzilate crop treated (see Table 7.2) by the percent of acre-treatments turning to dicofol if chlorobenzilate becomes unavailable, i.e., 2-10 percent (see text).

[d] For the probable case, dicofol residues are assumed to be approximately 5 times chlorobenzilate levels for citrus, other fruits, and nuts, i.e., chlorobenzilate residue times a 2.4 times greater application rate of dicofol, plus a 2 times greater residue persistence. An accumulation ratio of 0.33 is estimated for beef, lamb, and milk. See text for further discussion.

[e] For the worst case, dicofol residues are assumed to be 5 times the chlorobenzilate estimates for general U.S. population (see footnote *c*). For beef, lamb, and milk the same values as for the probable case are assumed since the Committee found no basis for making an alternative estimate to its probable-case estimate.

[f] For applicator exposure it was assumed that the exposure would be the same as for chlorobenzilate application times the 2.4 times greater application rate of dicofol (see text).

The daily dose from dietary routes is calculated by multiplying consumption times percent of crop treated times probable or worst-case residue.

[g] Only dermal and inhalation routes of exposure are included in the applicator estimates because for this population the exposure from these routes is so much larger than from their diet that the dietary exposure is insignificant.

[h] For flavored drinks the same residue estimate is used for the probable and worst cases, as for chlorobenzilate (see Table 7.2).

TABLE 7.8 Incremental Lifetime Dose per Individual of Dicofol by Regulatory Option for Chlorobenzilate[a]

Regulatory Option[b]	Daily Dose (m moles/kg)[c]		Duration[d]	Lifetime Dose (m moles/kg)[e]		Equivalent Chlorobenzilate Lifetime Dose (m moles/kg)	
	Probable	Maximum-Plausible		Probable	Maximum-Plausible	Probable	Maximum-Plausible
Citrus Ground Applicators (700)							
A	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0
C[f]	0	0	0	0	0	0	0
D	0.0025	0.0038	40 d/yr × 5 yr × 2-10%	0.01	0.053	0.03	0.17
E	0.0025	0.0038	40 d/yr × 10 yr × 2-10%	0.02	0.105	0.06	0.34
Florida Population (8×10^6)							
A	0	0	0	0	0	0	0
B[g]	0.084×10^{-9}	4.24×10^{-9}	365 d/yr × 10 yr	0.31×10^{-6}	15×10^{-6}	0.93×10^{-6}	47.8×10^{-6}
C[g]	0.084×10^{-9}	4.24×10^{-9}	365 d/yr × 10 yr	0.31×10^{-6}	15×10^{-6}	0.93×10^{-6}	47.8×10^{-6}
D[g]	0.084×10^{-9} 0.014×10^{-6}	4.24×10^{-9} 0.14×10^{-6}	365 d/yr × 5 yr	0.026×10^{-3}	0.26×10^{-3}	0.078×10^{-3}	0.83×10^{-3}
E	0.014×10^{-6}	0.14×10^{-6}	365 d/yr × 10 yr	0.051×10^{-3}	0.51×10^{-3}	0.152×10^{-3}	1.64×10^{-3}

General U.S. Population (except Florida) (212×10^6)

A	0	0	0	0	0	0	0
B[g]	0.084×10^{-9}	2.16×10^{-9}	365 d/yr × 10 yr	0.31×10^{-6}	7.8×10^{-6}	0.92×10^{-6}	24.7×10^{-6}
C[g]	0.084×10^{-9}	2.16×10^{-9}	365 d/yr × 10 yr	0.31×10^{-6}	7.8×10^{-6}	0.92×10^{-6}	24.7×10^{-6}
D[g]	0.084×10^{-9}	2.16×10^{-9}	365 d/yr × 5 yr	7.9×10^{-6}	0.10×10^{-3}	0.024×10^{-3}	0.32×10^{-3}
	4.24×10^{-9}	0.052×10^{-6}					
E	4.24×10^{-9}	0.052×10^{-6}	365 d/yr × 10 yr	0.015×10^{-3}	0.19×10^{-3}	0.045×10^{-3}	0.6×10^{-3}

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[a] Where estimates involve combining variables that are reported as ranges, the procedures described in Appendix F are used.

[b] Regulatory options:

- A. Continue registration of all uses.
- B. Cancel all noncitrus uses.
- C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions of registration to require protective clothing and respirators; cancel all other uses.
- D. Cancel chlorobenzilate use on citrus to take effect after 5 years, and in the interim apply Option C.
- E. Cancel all uses.

[c] Derived from Table 7.7.

[d] Dicofol applicators are assumed to be exposed only 2-10 percent of the time chlorobenzilate applicators are, since dicofol would be expected to replace chlorobenzilate in only 2-10 percent of chlorobenzilate's uses.

[e] Lifetime dose equals daily dose times duration.

[f] Assumes that volume of chlorobenzilate use will continue as at present.

[g] Assumes that dicofol will replace chlorobenzilate on noncitrus crops at same rate as it replaces chlorobenzilate on citrus.

chlorobenzilate is cancelled dicofol is assumed to replace chlorobenzilate for 2–10 percent of the current citrus acre-treatments, the product of the daily dose and number of days exposed is multiplied by 2–10 percent (see Table 7.8). This calculation assumes that the entire citrus applicator population will spray dicofol 2–10 percent of the time they would have sprayed chlorobenzilate, rather than a decreased applicator population doing all the dicofol spraying.

For dietary exposure estimates, the 2–10 percent replacement rate of dicofol for chlorobenzilate would be factored in by multiplying the extent of chlorobenzilate use on specific crops by 2–10 percent in the equation:

$$\text{Ingestion } (\mu\text{g/day}) = \text{consumption (g/day)} \times \text{extent of pesticide use on crop (\%)} \times \text{assumed residue (ppm).}$$

In this equation, food consumption will remain the same for dicofol as for the chlorobenzilate calculations. The range of assumed residues will differ, however.

For the Florida population, dicofol residue levels in meat and meat by-products from Florida beef and lamb and milk from the cattle are calculated using the accumulation ratio procedure recommended for chlorobenzilate. Only one estimate is calculated representing both the probable and maximum-plausible residue levels because the Committee found no basis for making an alternative estimate. The final daily dosage estimate is a range because the estimated replacement rate of dicofol for chlorobenzilate is a range.

It was necessary to derive an estimated accumulation ratio for dicofol in beef by indirect means, using various published data from beef and poultry experiments. Accumulation ratios for dicofol and DDT in poultry fat can be calculated using data from Fries (1969) and McCaskey *et al.* (1968). These values are 2 and 6, respectively. Similarly, an accumulation ratio of approximately 1 for DDT in beef fat can be calculated using data from Cummings *et al.* (1967). An estimated accumulation ratio for dicofol in beef fat can then be derived using the relationship:

$$\frac{\text{Dicofol accumulation ratio in poultry fat}}{\text{DDT accumulation ratio in poultry fat}} = \frac{\text{Dicofol accumulation ratio in beef fat}}{\text{DDT accumulation ratio in beef fat}}.$$

Inserting the calculated accumulation ratios into the above equation and solving for dicofol in beef fat gives:

Dicofol accumulation ratio in beef fat = 2/6 × 1 = 0.33.

An estimate of the maximum-plausible dicofol residue in citrus pulp can be derived by multiplying OPP's estimate of chlorobenzilate residue in pulp (2 ppm) times the greater application rate of dicofol (2.4×) (Bushong 1977) times the greater persistence of dicofol residues over chlorobenzilate residues (2–3×) (Carman *et al.* 1972, Gunther 1969). Dicofol residue in pulp is estimated to be approximately 10 ppm. The steady-state residue of dicofol in animal fat, then, is the accumulation ratio (0.33) × the concentration of dicofol in the diet (10 ppm in pulp × 16 lb of pulp ÷ 20 kg diet), or 0.33 × 3.6 = 1.19 ppm. Beef cuts averaging 30 percent fat (a maximum value) would contain 0.36 ppm residual dicofol. If Florida beef and lamb were consumed at a rate of 143.2 g/day (OPP's value), the estimate of daily dicofol ingestion by Floridians from this source would be 143.2 g/day × 2–10% dicofol replacement rate × 10% of chlorobenzilate crop treated × 0.36 ppm residue = 0.10–0.52 μg/day (see Table 7.7).

As with chlorobenzilate, estimates of dicofol residue concentrations in milk may be derived from the accumulation ratio approach described for beef. With dicofol residues in pulp at a level of 10 ppm, the resulting residue level in milk fat would be 1.19 ppm. This establishes a residue estimate of 0.042 ppm for milk containing 3.5 percent fat. If 184.7 g of milk were consumed daily (OPP's value), the estimate of dicofol ingestion would be 0.16–0.78 μg/day (see Table 7.7).

For the general U.S. population, the Committee's estimates of probable and maximum-plausible incremental daily doses of dicofol (resulting from replacement for chlorobenzilate) are based on the assumed residue levels of chlorobenzilate in citrus and noncitrus products multiplied by a factor of 5. This factor is rationalized as was done previously when estimating dicofol residues in citrus pulp, i.e., the greater application rate of dicofol (2.4×) times the greater persistence of dicofol residues (2–3×). Estimates of additional daily doses of dicofol for the U.S. population are shown in Table 7.7. For the Florida and general U.S. populations, total (lifetime) incremental exposure can be estimated by multiplying the daily dietary dose by the number of years dicofol would be expected to be used under the various regulatory options (see Table 7.8). Again, the Committee assumes an economic lifetime of 10 additional years for dicofol (see Chapter 4).

Pathological Activity of Dicofol The following assessment of the pathological activity of dicofol is restricted to its carcinogenic potential. The data for the calculations come from the 1978 NCI *Bioassay of Dicofol for Possible Carcinogenicity* (NCI 1978). The procedure recommended in Chapter 4 and illustrated in Appendix C was used to calculate the CAI for dicofol. Both high- and low-dose male mice showed statistically significant increases in hepatocellular carcinomas, although no statistically significant association between dose and mortality was observed. For the low dose, the CAI lies in the range 0.25–1.16 (using a 90 percent confidence interval) with a most-probable estimate of 0.86. For the high dose the range is 0.30–0.66 (using a 90 percent confidence interval) with a most-probable estimate of 0.55 (see Table 4.3). Since the low-dose test group developed a tumor yield of approximately 55 percent—which is comparable to the tumor yield in the Innes *et al.* (1969) chlorobenzilate study—the low-dose CAI estimate will be used in subsequent calculations.

Translating Dicofol Lifetime Exposures into Chlorobenzilate Exposure Equivalents

As noted earlier, to present the most useful information to a decision maker about the pesticide exposure for each affected population attendant to the various regulatory options, it is necessary not only to estimate exposure outcomes for the pesticide in question—in this case chlorobenzilate—but also to incorporate exposure to alternatives into the estimate. This is accomplished here by translating the lifetime exposure from dicofol (Table 7.8) into chlorobenzilate exposure equivalents using the method described in Chapter 4 (see the section on Combining Exposure and Pathological Activity).

Chlorobenzilate exposure equivalents for dicofol are shown in the last column of Table 7.8. The uncertainty associated with the CAI values for dicofol and chlorobenzilate was taken into account as described in a footnote to the table. The chlorobenzilate exposure equivalents for dicofol will be combined with the chlorobenzilate exposure values in Table 7.6 in the final major section of this chapter, to produce a single exposure estimate for each population segment under the various regulatory options (see Table 7.26).

Reference Compounds

The implications of lifetime exposures expressed in millimoles per kilogram of body weight are hard to perceive. To gain an appreciation of the effects on public health of using chlorobenzilate it is, therefore, virtually essential to compare its carcinogenic potency and anticipated dose levels with those of other pesticides that have been considered extensively and have been subjected to regulatory decisions. The chlordane-heptachlor complex is well suited to this purpose. Their chemical structures and metabolic behavior in mammals are roughly similar to those of chlorobenzilate. Laboratory experiments under comparable test conditions and within comparable parameters are available for chlordane, heptachlor, and chlorobenzilate (see Table 4.3). The uses of all three compounds in agriculture and the resultant patterns of exposure are roughly similar. The nature of the principal risk to public health that chlordane and heptachlor present—cancer—is identical with that of chlorobenzilate.

The registrations of both chlordane and heptaclor for most uses were suspended in 1975 on the grounds that "the human cancer hazard posed by these pesticides and the lack of benefits to outweigh this risk were the bases for their suspension" (CEQ 1976:31). Their registrations were cancelled after further investigation in March 1978.

Some determinations of the CAI's for both chlordane and heptachlor are included in Table 4.3. Since the CAI adopted for chlorobenzilate is derived from experiments with male mice (females appear to be less sensitive), the determinations for chlordane and heptachlor derived from experiments with males are the relevant ones for comparison. There is only one such determination for heptachlor, giving a CAI of about 19. There are five determinations for chlordane using males at five different dose levels. At the lowest concentration, 5 ppm, the indicated CAI was 3.1, but the observed rate of excess tumor response was so low that the estimate is not reliably greater than zero. At higher dosages, the indicated percent of animals in which tumors were induced by administration of chlordane were 80 percent at 25 ppm and slightly less, but not enough to be statistically significant, at the higher doses. We infer that a substantial increase in tumorgenesis is induced by the administration of 25 ppm of chlordane, but that thereafter any increase in responses is too gradual to be detected by samples of the size used in the experiments reported. Accordingly, we have adopted a CAI of 14.5, corresponding to the 25 ppm dose level of chlordane.

These estimates of carcinogenic activity are displayed graphically in

Figure 7.1, which shows the accompanying uncertainty, and they are used in the evaluation in the last section of this chapter.

AN ECONOMIC EVALUATION OF THE BENEFITS

This section applies the principles and recommendations set forth in Chapter 5 to assess the benefits of using chlorobenzilate. Since OPP has previously completed a benefit assessment for chlorobenzilate (Luttner 1977a, b), the discussion in this section will employ many of the data compiled for the OPP analysis.

The preliminary benefit analysis by OPP (Luttner 1977a) estimated that 1.1 million lb of chlorobenzilate were applied in 1975 (the base year for the analysis). Most of this chlorobenzilate, approximately 920,000 lb, was applied to control the citrus rust mite on Florida and Texas oranges and grapefruit and the citrus bud mite on Arizona and California lemons. Another 76,000 lb were used on other citrus crops (e.g., limes and tangelos). Cotton farmers made slight use of chlorobenzilate, applying around 39,000 lb. Finally, the remaining 81,000 lb were sprayed on a wide variety of fruits, nuts, and other miscellaneous crops. The analysis in this section will be restricted to the major uses of chlorobenzilate, namely, mite control on oranges, grapefruits, and lemons.[2]

The presentation is divided into three parts. The effects of chlorobenzilate use on yield and quality of citrus are discussed in the first part. Estimates of the effect that chlorobenzilate use has on pest control costs in the citrus industry are presented in the next part. Finally, the estimated yield, quality, and cost effects are translated—with the aid of conventional benefit-cost analysis—into overall estimates of the benefits of chlorobenzilate use (or, alternatively, of the benefits forgone because of withdrawal of chlorobenzilate from the market).

EFFECTS ON YIELD AND QUALITY

The OPP preliminary benefit analysis (hereafter, PBA) adopts a number of important assumptions concerning effects on yield and quality likely to be associated with the loss of chlorobenzilate. Briefly, the OPP analysis assumes that the available alternative miticides will " . . . provide yields and product quality comparable to chlorobenzilate . . . " (Luttner 1977a:45a). However, it also assumes that failure to treat for mites would have significant adverse effects on fruit size, appearance, crop yield, and tree-stock stamina (Luttner 1977a:44). This section considers each of these key assumptions.

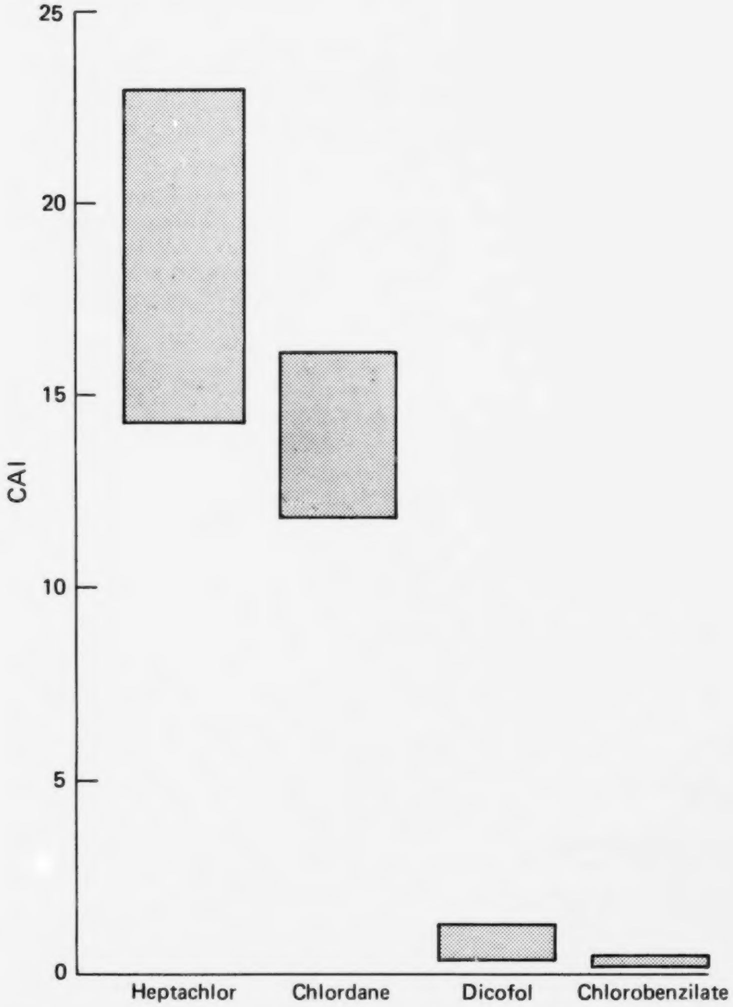

FIGURE 7.1 CAI's used in Chapter 7 calculations (see section on "Estimation of Risk Under Various Regulatory Options" in this chapter) with confidence intervals for chlorobenzilate, dicofol, and the selected comparison compounds. Source: Table 4.3.

No Miticide Treatments

If chlorobenzilate were not available, citrus growers would have the choice of either treating with an alternative miticide or not treating at all. Consideration of the no-treatment option led OPP to the following conclusion (U.S. EPA 1978a:44–46):

> . . . uncontrolled mites cause reductions in fruit size of 12% for oranges and 17% for grapefruit. Fruit size declines also occur in lemons, but these effects have not been fully quantified. Also, overall yield can be reduced by mite infestations due to fruit drop (Allen 1978). It is estimated that such reductions in fruit size and overall yield would reduce grower gross revenues by about $159 million per year (approximately 16 percent of total industry revenue).

These estimates are supported by data developed by Allen (1978) and brought to OPP's attention by USDA's assessment team for chlorobenzilate.[3] A subsequent search of the literature revealed that the USDA assessment team failed to bring to OPP's attention eight additional studies of the effect of chemical miticides on citrus yields. None of these additional studies—which are summarized in Table 7.9—found a statistically significant difference in yields between sprayed and unsprayed plots that could be attributed to rust mites.

The largest percentage decrease in yield (23 percent) was measured by Reinking (1967), but it was not statistically significant because of the great variability in yield between trees. Simanton (1962) and Griffiths and Thompson (1953) found 20 percent decreases; Griffiths and Thompson's finding was not statistically significant, however, and Simanton did not report a significance test. In no case did the unsprayed trees have greater yields than the sprayed ones, so that the possibility of some decrease cannot be ruled out. If there is a decrease, however, it is too small to be detected by any of the experiments found in the Committee's search of the literature.

Allen and Stamper (1979) examined the frequency distribution of citrus rust mite damage on citrus fruit and concluded that the effect of russetting was not serious until 50–75 percent of the surface was russetted. Generally, less than 5 percent of the oranges and 40 percent of the grapefruit in unsprayed groves were heavily scarred by rust mite. Allen (1978) found that the drop rate of fruit scarred by rust mite did not increase above that of unscarred fruit unless 75–80 percent of the surface skin was russetted. Allen (1979) also found that weight of citrus fruit decreased with 50 percent or greater scarring, while the percentage of total soluble solids increased in proportion to the amount of rust mite damage. It was also found that grapefruit achieved a smaller diameter when more than 87.5 percent of the surface was scarred. All of the above effects were attributed to increased water loss from scarred fruit.

Irrigation of citrus groves with citrus rust mite infestation would alleviate some of the problems of water loss caused by severe russetting. In Florida, 78 percent and 72 percent, respectively, of the orange and grapefruit acreage is irrigated, while all of the bearing citrus acreage in Texas and California is irrigated (U.S. FEA 1976). In fact, oranges with rough lemon rootstock, with its extensive root system and greater water-gathering capacity, are less affected by rust mite damage than orange trees with less extensive root systems (Allen 1979).

McCoy *et al.* (1976b) found that 20–30 percent of the outside surface of oranges could be damaged by rust mite with no effect on yield of fruit. They also found that if extensive damage (50 percent of all the fruit in a grove with extensive surface bronzing) occurred, the fruit could either be harvested early or irrigated to prevent excessive moisture loss and peel shrinkage.

McCoy (1976) analyzed the effects of rust mites on leaves in Valencia orange groves. He concluded that uncontrolled mite populations could cause a 3 percent increase in leaf drop, but this would not be severe enough to affect the vigor of the tree or its subsequent yield. Again, he suggested irrigation, a common practice in Florida, as a means of controlling this problem.

Van Brussel (1975) analyzed the interrelation of greasy spot and rust mite in citrus groves in Surinam. He found that trees with heavy rust-mite and greasy-spot infestations suffered defoliation, while trees with higher levels of rust mites that were sprayed to control greasy spot did not show any signs of defoliation. He concluded that greasy spot was the agent responsible for leaf drop in citrus.

Another study by McCoy (1977) found that unsprayed orange groves had 16–38 percent of the fruit damaged by rust mites, while groves sprayed with chlorobenzilate had 1–8 percent of the fruit damaged. McCoy's previous work (1976a, b) and work by Allen (1978, 1979) indicated that this level of damage to an unsprayed grove would probably not cause a decrease in fruit or juice yield.

Yothers (1918) presented data indicating that russetted oranges and grapefruit were 10–17 percent smaller than clear fruit. However, his data did not reveal the yield or russetting differences between sprayed and unsprayed plots. Moreover, Sinclair (1972) found that, on the basis of fruit volume, smaller grapefruit yielded significantly more juice than larger fruit. Apparently, the peel affects the percentages by volume more than the percentages by weight.

TABLE 7.9 Yields of Citrus in Sprayed and Unsprayed Plots

State	Crop	Yield		Significance[a]	Source
		Spray	No Spray		
Florida	Valencia oranges	2.9 boxes/tree	2.9 boxes/tree	NS	Griffiths and Thompson (1953)
Florida	Seedy grapefruit	10.0 average; 13.4 expected average of boxes/tree	8.7 average; 10.8 expected average of boxes/tree	NS	Griffiths and Thompson (1953)
Texas	Oranges	126 lb/tree	123 lb/tree	NS	Reinking (1967)
Texas	Grapefruit	372 lb/tree	285 lb/tree	NS	Reinking (1967)
Florida	Oranges	201 boxes/acre	201 boxes/acre	NS	Simanton (1962)
Florida	Grapefruit	307 boxes/acre	245 boxes/acre	?[b]	Simanton (1962)
Florida	Tangerines	310 boxes/acre	310 boxes/acre	NS	Simanton (1962)
Florida	Oranges	3,896 lb solids/acre	3,500 lb solids/acre	S[c]	McCoy et al. (1967a)

[a] Mite infestation yield reduction.

[b] Undetermined by author.

[c] This study did find a statistically significant yield reduction; however, this lower yield was caused by greasy-spot fungus infestations and not by mite infestations.

The weight of all this evidence supports the conclusion that the economic value of chlorobenzilate treatments of citrus fruits is far less than the estimate of $159 million a year adopted by OPP. (OPP's quantitative estimate is based only on yield effects; it does not consider the impact on consumer demand of cosmetic effects from not treating.) However, for purposes of estimating this value, it is misleading to compare the yields and qualities of orchards treated with chlorobenzilate with those of orchards where no protective measures have been taken. Citrus rust and bud mites are perceived by most growers and citrus entomologists as major pests. Relatively economical alternatives to chlorobenzilate are available. Consequently, growers will almost certainly continue to treat for mites, either with chlorobenzilate or with an alternative.

Alternative Miticide Treatments

The OPP assumption that the alternatives will provide yields and product quality comparable to that provided by chlorobenzilate was both plausible and acceptable to the USDA assessment team (J. Knapp, University of Florida Extension Service, Gainesville, personal communication, December 1978). A number of relevant studies lend support to the assumption.

For instance, in a study of Texas orange and grapefruit groves, Reinking (1967) analyzed the effect of oil on citrus pests. Although he stated that the correct grade of oil controls Texas mites, during the periods of his study neither the experimental nor the control plots contained significant mite populations. More importantly, however, he found that the correct grade of oil did not injure the trees or affect the yield and quality of fruit.

Jeppson *et al.* (1955) analyzed the effects of chlorobenzilate and oil in the control of the citrus bud mite and the citrus red mite in California. They found that when chlorobenzilate was used, 20 percent of the buds became infested with bud mite, while 32 percent of the buds were infested when petroleum was used. However, petroleum sprays effectively controlled the red mite, while chlorobenzilate was relatively ineffective.

Townsend (1976) analyzed 2 years of integrated pest management (IPM) programs in Florida orange groves. In the IPM groves, oil was used to suppress mite populations, but in some instances, large mite populations were treated with chlorobenzilate. In the fall only a few groves along the ridge were sprayed for rust-mite control, while none of the groves along the east coast of Lake Okeechobee needed mite control for late russetting or bronzing. Oil was also found to suppress greasy-spot fungus at low fungal densities. The IPM demonstration blocks, using little chlorobenzilate, had rust-mite densities 2 times greater than the conventional plots with no reduction in yield or soluble solids.

McCoy *et al.* (1976a) also examined a reduced pesticide program for pest control in Florida orange groves. Three spray programs were analyzed over a 4-year period: (1) conventional; (2) IPM; and (3) no spray. The IPM blocks received, on average, 1.2 fewer sprays for rust mites per year than the conventional blocks and showed no more rust-mite activity than the control. The unsprayed blocks also showed no increase in late rust-mite damage over the 4-year period. Yields in the unsprayed plot were reduced by greasy-spot fungus and dry weather.

Under humid growing conditions, the fungus *Hirsutella thompsonii* controls citrus rust-mite populations. McCoy *et al.* (1976a) found that in the unsprayed plots this fungus effectively controlled citrus rust mite over a 4-year period. Indeed, the fungus thrived in the unsprayed plots compared to sprayed plots. Townsend (1976) stated that *H. thompsonii* controls the citrus rust mites when mite populations reach high densities in July and August. McCoy *et al.* (1971) reported suppression of citrus rust-mite populations, equal to that achieved through the use of chlorobenzilate, with a 5 percent spray of the fragmented mycilia of *H. thompsonii*. The investigators stated that their methods worked well at high levels of mite infestation and under humid conditions. They did not determine whether this process was economical or whether it would control subeconomic mite populations (i.e., populations for which the cost of treatment exceeds the losses from not treating). Van Brussel (1975) also achieved excellent rust-mite control in Surinam using *H. thompsonii* as a biological control agent. Chlorobenzilate has been found to cause a 50–60 percent reduction in entomopathogenic fungi (Olmert and Kenneth 1974), and thus it can interfere with control of citrus rust mite by *H. thompsonii*.

In summary, the evidence indicates that the yield and quality of citrus crops will not be diminished appreciably, if at all, if farmers are required to replace chlorobenzilate treatments with some alternative.

CHANGES IN PEST CONTROL COSTS

To estimate the change in pest control costs (ΔPC) that cancellation of chlorobenzilate's registration would occasion, it is necessary to develop measures for several variables. The requisite information is indicated by an examination of the operational definition of ΔPC relevant to a cancellation. For any specific region and type of citrus,

$$\Delta PC = \sum_{j=1}^{J} \Delta[A_j T_j(MC_j + AC_j)] - \sum_{k=1}^{K} [A_k T_k(MC_k + AC_k)]$$

where j denotes one of J (nonchlorobenzilate) pest control methods used on citrus; k denotes one of K spray mixtures containing chlorobenzilate (e.g., chlorobenzilate-sulfur); A_j and A_k denote acres treated per year by method j or k, respectively; T_j is the average number of treatments per year by method j, and T_k is defined similarly; MC_j and MC_k are material costs per acre-treatment; AC_j and AC_k are application costs per acre-treatment; and Δ denotes the change in the variable or expression that follows it that would be induced by cancelling the registration of chlorobenzilate for the specific use being analyzed.

In implementing this measure, it is assumed that total citrus acreage remains constant. The assumption is not crucial to estimating the change in production costs per unit of output (the ultimate objective of this section), and it will be relaxed in the next section.

The expression $\Delta[A_j T_j(MC_j + AC_j)]$ is the change in expenditures on control method j (which might be a nonchemical method) arising from the cancellation of chlorobenzilate. Usually (but not always) this term will equal zero (when total acreage is held constant), unless the pest control method itself provides an alternative to the use of chlorobenzilate. Presumably, for the alternatives this term will be positive or zero.

In order to estimate ΔPC occasioned by the denial of chlorobenzilate, it is necessary to have information on each of the variables in the equation. In the next section we discuss OPP's approach to quantifying the expected ΔPC in the event that chlorobenzilate's registration for use on citrus is cancelled. We then discuss and implement some alternative measures for some of the components of ΔPC.

Data and Assumptions

The main source of the data used by OPP for measuring ΔPC is the Doane Specialty Crops Study for the years 1972, 1973, and 1974 (reported in Luttner 1977a). The Doane report provided estimates by state and type of citrus for acres treated with various miticides, average number of treatments per year, application rate per acre-treatment, and the unit cost of the miticides (e.g., dollars per gallon). These statewide estimates are based upon samples of citrus growers in the various states (approximately 300 in Arizona-California, 375 in Florida, and 200 in

Texas: E. Dixon, Doane Agricultural Service, Inc., St. Louis, Mo., personal communication, November 1978). OPP supplemented these data from Doane with information from published and unpublished papers, personal communications with citrus experts, and the report submitted by the USDA assessment team for chlorobenzilate (USDA 1977b).[4] In the following discussion, the specific sources of the data used by OPP for each variable are identified.

1. The *K* currently used miticide spray combinations containing chlorobenzilate are obtained from the Doane survey. The PBA considers four chlorobenzilate combinations for oranges, two for lemons, and seven for grapefruit (Luttner 1977a:50–52).

2. The *J* pest control methods that would be more widely used following a chlorobenzilate cancellation were identified in several ways. Identification of the relevant alternatives to chlorobenzilate was based upon three criteria. To be classified as an alternative for use on a specific type of citrus in a state, actual use of the chemical had to be reported in the Doane survey, the chemical had to be listed among recommended miticides in the state's citrus guide, and it had to be identified by state entomologists as an alternative likely to be used in place of chlorobenzilate (Luttner 1977a:48). The number of alternatives, according to state and type of citrus is (Luttner 1977a:50–52):

	Oranges	Grapefruit	Lemons
Arizona	NA	NA	3
California	NA	NA	1
Florida	5	7	5
Texas	7	5	NA

NA = Not applicable, because no chlorobenzilate use was reported for this site.

In addition, the Supplement to the PBA (hereafter, S-PBA) concluded that loss of chlorobenzilate would eventually occasion increased use of *scalicides* in Florida because the alternative miticides most likely to be used are lethal to insects parasitic on scale (Luttner 1977b).

3. Data on the average number of applications (*T*) per year for miticides are available from the Doane survey. However, with one exception, the PBA does not use these estimates of *T*; rather, the PBA generally assumes that *T* for each of the alternatives is the same as the

average T for the various chlorobenzilate mixtures relevant to a use site. The one exception is the use of oil on California lemons; in this case, T is set equal to 2 (a value consistent with the Doane survey) for two thirds of the California lemon acreage (Luttner 1977b:9), rather than 1 as is assumed for chlorobenzilate mixtures used on California lemons. The assumption that T is the same for virtually all the miticide mixtures (chlorobenzilate mixtures and substitutes) considered is not supported by the data in the Doane survey. OPP's estimates of T for the Florida scalicides are based upon information provided in the USDA assessment team report (USDA 1977b), hereafter abbreviated USDA-ATR.

4. OPP's estimates of base acres treated (A_k) with any one of the chlorobenzilate mixtures are taken from the Doane survey (Luttner 1977a).

5. For the most part, OPP assumes that the total number of acres treated with miticides would not be affected by a regulatory action against chlorobenzilate. Specifically, for miticide treatments in Arizona, Florida, and Texas, it is assumed that $\Sigma_j \Delta A_j = \Sigma_k A_k$. The exception occurs in connection with California lemons: to account for the claim in the USDA-ATR that cancellation of chlorobenzilate would lead to an increase in the number of acres requiring treatment, OPP inferred that base acres treated would grow to 41,000 (after 5 years) from the current 5,000 (Luttner 1977b:9). In addition, OPP inferred (also from relatively general statements in the USDA-ATR) that the loss of chlorobenzilate would so hamper the IPM program in Florida that all the Florida citrus acreage (around 850,000 acres) would require two additional scalicide treatments (Luttner 1977b:6).

6. The OPP estimates of acre-treatments for the various chlorobenzilate mixtures ($A_k T_k$) are easily constructed from the data provided by Doane on base acres and average number of treatments (Luttner 1977a:51–53, 114–128).

7. With the exception of California lemons, the change in total acre-treatments for the alternatives is taken as equal to the total acre-treatments for the chlorobenzilate mixtures. That is, OPP generally assumes that for the alternatives, $\Sigma_j \Delta A_j T_j = \Sigma_k A_k T_k$ (see, e.g., Luttner 1977a:50–52). For California lemons, acre-treatments are assumed to expand (after 5 years) to 68,470 from 5,000 with chlorobenzilate—an estimate dependent upon the assumption that 41,000 acres would require at least one additional treatment of oil (as a replacement for chlorobenzilate) and two thirds of those 41,000 acres would require two additional oil treatments per year (Luttner 1977b:9). The additional acre-treatments for the scalicides in Florida are estimated by OPP to be 1.7 million after 5

years (850,000 acres × 2 additional treatments per year [Luttner 1977b:8]).

8. OPP estimated the anticipated change in acre-treatments for any specific alternative (with the exception of oil on California lemons) by simply dividing the estimate of the change in total acre-treatments by the number of viable alternatives (Luttner 1977a:50):

$$\Delta A_j T_j = \frac{\sum_j^J \Delta A_j T_j}{J} .$$

The estimation of additional acre-treatments for oil on California lemons and for scalicides in Florida was discussed above.

9. OPP estimated material costs per acre-treatment (*MC*) for the chlorobenzilate mixtures and the alternatives in two different ways. Estimates for *MC* for all of the various chlorobenzilate mixtures and alternatives are available from the Doane report. However, in some cases " . . . the expenditure data in the Doane material were perceived (by OPP) as being either excessively low or high . . . " (Luttner 1977a:48). In such instances, the expenditure per acre-treatment was derived by using prices from current pesticide price lists and the recommended application rates reported in the state citrus guides (Luttner 1977a:50–52). OPP's estimate of *MC* for the additional scalicide treatments in Florida is based upon information provided by the assessment team (Luttner 1977b:8).

10. The PBA generally assumes that the application costs per acre-treatment are the same for all of the chlorobenzilate mixtures and the alternatives (Luttner 1977a:50–52). Consequently, this cost element is ignored (except in the case of California lemons and scalicide treatments in Florida) in estimating the change in treatment costs that cancellation of chlorobenzilate would occasion. That is, the estimate of ΔPC costs is collapsed to:

$$\Delta PC = \sum_j^J \Delta A_j T_j(MC_j) - \sum_k^K A_k T_k(MC_k) .$$

The OPP estimates of application costs per acre-treatment for the oil sprays on California lemons and scalicide treatments on Florida citrus are based on information provided in the USDA-ATR.

The OPP estimates for the change in annual pest control costs that are likely to occur if chlorobenzilate is withdrawn are shown in Table 7.10. The total is $57.6 million.

TABLE 7.10 OPP's Estimated Change in Annual Pest Control Costs on Citrus Following Cancellation of Chlorobenzilate[a] (in thousands of 1975 dollars)

	Type of Citrus			
State	Grapefruit	Lemons	Oranges	Total
Arizona	—	$ 0	—	$ 0
California	—	$4,821[b]	—	$ 4,821
Florida				
Non-IPM	$ 468	$ 34	$ 1,541	$ 2,043
IPM	$8,570[b]	$ 398[b]	$41,523[b]	$50,491
Texas	$ 44	—	$ 230	$ 274
Total	$9,082	$5,253	$43,294	$57,629

[a] These estimates are from Luttner (1977a; pp 50-52; 1977b, pp. 9, 12).
[b] These estimates apply to the fifth year following withdrawal of chlorobenzilate.

The extent to which OPP's overall benefit estimate is highly dependent upon two key assumptions is demonstrated through the sensitivity analysis in Table 7.11. Clearly, these crucial assumptions by OPP concerning Florida scalicide treatments (accounting for 87.6 percent of the total benefits) and bud-mite control on California lemons (accounting for 8.4 percent of the total) require scrutiny. We shall review, in order, the impacts of disallowing the use of chlorobenzilate on (1) the Florida IPM program, (2) bud-mite control on California lemons, and (3) mite control on Arizona, Florida (non-IPM effects), and Texas citrus.

Florida IPM *Effects* Currently, the most important Florida citrus pests are citrus rust mite, greasy-spot disease, and citrus snow scale. Before 1960, purple scale and Florida red scale were also major pests of citrus. However, the introduction of two hymenopterous parasites, *Aphytis lepidosaphes* and *A. holoxanthus*, relegated these two scale insects to the role of minor pests on all the Florida citrus acreage (Brooks 1977:31). In addition, Florida entomologists are currently attempting to establish a third parasite, the Hong Kong wasp (*A. lingnanensis*), to provide control over citrus snow scale (Luttner 1977b:2). An important advantage of chlorobenzilate is its specificity to mites: it has little deleterious effect upon the parasites used to control these scale insects.

The OPP analysis assumes that the alternatives to chlorobenzilate

TABLE 7.11 Contribution of Key Assumptions to OPP's Estimate of Annual Benefits from Chlorobenzilate Use

I. OPP's estimate of annual benefits	$57,629,000
II. Key assumptions underlying benefit estimate	
A. Cancellation would disrupt the Florida IPM program leading to two additional scalicide treatments on all Florida citrus acreage (850,000 acres) at a per acre cost of $10.08 for materials and $19.62 for application:	$50,491,000 (87.6 percent of total)
B. Cancellation would result in acre-treatments for bud-mite control in California expanding to 68,470 from the present 5,000. Per acre-treatment costs with chlorobenzilate average $76.60 (including application costs), whereas the alternative (oil) averages $76 (including a $40 application cost). Thus, the net cost increase is:	$ 4,821,000 (8.4 percent of total)
Overall contribution of the two assumptions:	$55,312,000 (96.0 percent of total)

Source: Derived from Luttner (1977a,b).

would destroy the hymenopterous parasites of the scale insects. "This situation would result in a return to the pre-IPM scale insect control practices . . . in which two dilute scalicide sprays were applied to all of the commercial Florida citrus acreage each year" (Luttner 1977b:3). However, this assumption appears to be unrealistic.

The PBA identifies the major alternatives to chlorobenzilate in Florida as dicofol, ethion, oil, and sulfur. Dicofol and oil have little deleterious effect on the beneficial insects, so use of these two alternatives would certainly not be disruptive of the IPM program. (The use of dicofol in groves infested with snow scale can create complications, however; this point is discussed below.)

Both ethion and sulfur are toxic to the scale parasites. However, effects of these two pesticides are relatively short-lived (USDA 1977b:Attachment V). Consequently, while an ethion or sulfur treatment may destroy most of the adult scale parasites in a grove, it will not prevent the progeny from reestablishing the predator population. In fact, the *Florida Citrus Spray and Dust Schedule 1977* (University of Florida 1977) recommends a summer application of ethion and oil, and expresses no concern that such an application will interfere with the natural control of purple and Florida red scale. Of course, frequent or excessive applications (especially of sulfur) would eventually destroy the *Aphytis* populations (J. Knapp, University of Florida Extension Service, Gainesville, personal communication, December 1978).

The key to continued natural control of the scale insects lies in the avoidance of frequent applications of materials toxic to the parasite populations. Since most citrus groves in Florida receive only two to three spray or dust applications a year (USDA 1977b:Attachment XII,1), the maintenance of the predator populations would appear to be a feasible goal, contrary to the conclusion reached by OPP.

As noted above, the use of dicofol is consistent with natural control of purple and Florida red scale. However, dicofol treatments can produce abnormally high populations of citrus snow scale (Brooks and Whitney 1977:431). Consequently, the *Florida Citrus Spray and Dust Schedule 1977* recommends that dicofol be combined with a scalicide for use in groves infested with citrus snow scale. This evidence clearly supports OPP's view that " . . . the projected overall increase in use of dicofol following a cancellation of chlorobenzilate would also increase the use of scalicides for snow scale control" (Luttner 1977b:3).

The relevant issue, of course, is: how costly would these additional scalicide treatments be? Approximately 45 percent of Florida citrus groves (perhaps 350,000 acres) harbor snow scale, and about 25 percent of the groves suffer economic infestations requiring treatment (Brooks and Whitney 1977:427). Thus, dicofol treatments could aggravate the snow-scale problem on about 350,000 acres. However, approximately 200,000 of these acres are already being treated for snow scale. These treatments are assumed in the Committee's analysis to be adequate to handle any problems created by the use of dicofol. Only those 150,000 acres with noneconomic infestations would require additional scalicide treatments as the result of using dicofol.

The Committee assumes that the scalicide (material) cost per acre-treatment is $10.00 (the S-PBA reports scalicide costs ranging from $5.00 to $12.66 per acre-treatment). According to the *Florida Citrus Spray and Dust Schedule 1977*, the scalicides can be applied along with dicofol. However, the application of a scalicide—complete coverage of all wood is essential—will increase the amount of water used per acre and increase the time required to spray each acre (J. Knapp, University of Florida Extension Service, Gainesville, personal communication, December 1978). The additional application cost is assumed to be $10.00 per acre-treatment (the S-PBA estimates the application cost for an entire additional treatment to be $19.62 per acre).

If we assume that loss of chlorobenzilate would result in one additional dicofol treatment on all acreage currently harboring noneconomic infestations of snow scale (an assumption that would produce a maximum-plausible estimate of the benefits of chlorobenzilate use), then the additional *scalicide* costs would be about $3 million per year. For a minimum-plausible estimate of chlorobenzilate benefits, we adopt the assumption that chlorobenzilate's role in the IPM program can be assumed by an alternative (such as oil), thereby mitigating the snow-scale complication. Under this assumption there would be no cost effects peculiar to the IPM program, so assessment of any cost increases related to the use of higher cost alternatives can appropriately be included in a subsequent section dealing with non-IPM cost effects in Florida (and other states).

In summary, the Committee's appraisal of the effect of disallowing chlorobenzilate on the cost of combatting snow-scale infestation is in the range $0–$3 million a year, far lower than OPP's estimate of $50 million.

Bud-Mite Control on California Lemons According to the USDA-ATR (USDA 1977b), there are about 41,000 lemon acres in California that could require treatment for bud mites. However, in any given year only about 5,000 acres require treatment with chlorobenzilate, with the acres being treated possibly changing each year. Loss of chlorobenzilate would leave oil as the only registered alternative for treatment of bud mites on California lemons.

Dr. Glen Carman, a University of California entomologist, reports in the USDA-ATR (USDA 1977b:2, California section) that " . . . much of the lemon acreage in the citrus bud mite areas will receive one petroleum oil treatment a year for other pest control purposes." He further notes that "dependence upon petroleum oil sprays for the control of citrus bud mite would be expected to result in the mandatory use of one petroleum oil treatment each year in all bud-mite-infested properties and both a spring and a fall treatment in some localities or during some seasons."

As a maximum-plausible case assumption, we accept OPP's assessment that all 41,000 acres would require one mandatory treatment with oil for bud-mite control and that 27,500 of those acres would require two treatments with oil (USDA 1977b). However, we also allow for the fact that virtually all of these acres already receive at least one treatment of oil for other purposes. Consequently, loss of chlorobenzilate (under these assumptions) would lead to 27,500 additional acre-treatments with oil.

On the basis of information provided by Carman in the USDA-ATR, material costs are taken as being $33.02 per acre-treatment (26 gal/treatment at $1.27/gal). We assume that this oil can be included in spray mixes that would be applied in any event; consequently, application costs for the additional oil treatments are assumed to be zero. In fact, Carman notes that this additional oil treatment would probably supplant an existing spring (nonchlorobenzilate) treatment for red mites, since oil provides some control for this type of mite (Dr. Glen Carman, University of California, Riverside, personal communication, November 1978).

This set of maximum-plausible case assumptions implies that loss of chlorobenzilate for bud-mite control on California lemons would occasion increases in pest control costs equal to $870,000 ($910,000 for oil less the $40,000 currently spent on chlorobenzilate). Of course, the estimate may overstate the costs, because it fails to account for any cost savings occasioned by the substitution of oil for chlorobenzilate in treating red mites.

To make minimum-plausible estimates of the benefits of chlorobenzilate use, we assume that each chlorobenzilate treatment can be replaced with a single treatment of oil so that total acre-treatments remain at 5,000. In this instance, the loss of chlorobenzilate would occasion additional treatment costs of $125,000. OPP, using somewhat different assumptions, estimated the increase in pest control costs at $4.8 million a year.

Other Cost Effects In this section we estimate the changes that loss of chlorobenzilate would occasion in the cost of controlling citrus pests in Arizona, Florida, and Texas. The discussion concerning Florida citrus focuses on those cost effects that would be independent of the IPM program. We proceed in this section by considering the Committee's assumptions and the types of information needed to implement the measure of ΔPC.

1. The list of K spray mixes containing chlorobenzilate that are currently used on citrus is taken from the Doane survey (Luttner 1977a).
2. The pest control methods (in this instance, they are all alternatives) that would probably be more widely used following a loss of chlorobenzilate are selected by merely adopting the list of alternatives (and the selection criteria) employed in OPP's analysis. The various alternatives to chlorobenzilate are listed in Table 7.12.
3. Information concerning the average number of treatments per year for chlorobenzilate and the alternatives is also presented in Table 7.12. The data in the table reveal that—contrary to OPP's assumption—the average number of treatments with chlorobenzilate mixtures may differ from the treatment rate for the alternatives. Consequently, in estimating

TABLE 7.12 Average Number of Miticide Treatments Per Year: Chlorobenzilate and Alternatives

	Doane Report				USDA-ATR
Miticide	Oranges	Grapefruit	Lemons	Weighted Average	Citrus
Florida					
Chlorobenzilate (all mixtures)	1.24	1.14	1.17	1.22	1.28-2.10
Alternatives					
Oil	1	1	NR	1	1.40-1.71
Sulfur	1.2	1.3	NR	1.25	1.60
Ethion	1.1	1	NR	1.05	1.14-1.38
Dicofol	1	1	NR	1	1
Ethion/sulfur	—	1	—	1	NR
Ethion/oil	1	1	1	1	NR
Dicofol/sulfur	—	1	—	1	NR

Arizona					
Chlorobenzilate			1		
Alternatives					
Dicofol			1		
Ethion			NR		
Sulfur			1		
Texas					
Chlorobenzilate (all mixtures)	1.54	1.58		1.56	2.5
Alternatives					
Ethion	NR	2.0		2.0	4.0
Dicofol	NR	—		—	2.5
Carbophenothion	1.5	1.9		1.8	2.0
Ethion/oil	2.7	2.0		2.3	NR
Carbophenothion/oil	1.8	1.4		1.6	NR
Dicofol/oil	—	3.0		3.0	NR
Propargite	NR	—		—	NR
Fenbutatin-oxide	NR	—		—	NR

Note: NR indicates not reported; dashes denote miticides that are not likely alternatives.
Source: Luttner (1977a) and USDA (1977b).

TABLE 7.13 Acres Grown and Base Acres Treated With Chlorobenzilate, by State and Type of Citrus

	Type of Citrus					
	Grapefruit		Lemons		Oranges	
State	Acres Grown	Acres Treated	Acres Grown	Acres Treated	Acres Grown	Acres Treated
Arizona	9,700	0	19,200	2,000	22,000	0
California	20,700	0	52,800	5,000	180,700	0
Florida	132,000	107,000	7,600	6,000	640,000	416,000
Texas	42,000	22,000	100	0	34,000	15,000

Source: Doane Specialty Crop Studies for 1972, 1973, and 1974 (reported in Luttner (1977a)) and U.S. Department of Commerce (1978, Vol. II, Part 6, pp. 118-119). Data on lemon acreage in all states and grapefruit and orange acreage in Arizona and California are from U.S. Department of Commerce (1978).

cost effects of a chlorobenzilate cancellation, we examine the implications of replacing OPP's measure of treatment rates (no difference between the chlorobenzilate mixes and the alternatives) with the measures provided in Table 7.12.

4. Following OPP's lead, our estimate of base acres treated (A_k) with any one of the chlorobenzilate mixes is taken from the Doane report. Table 7.13 presents information on base acres treated annually with chlorobenzilate, by state and type of citrus. To provide some perspective on the relative extent to which chlorobenzilate is used, Table 7.13 also reports acres grown for each type of citrus.

5. In this part of the analysis, we assume—as did OPP—that total acres requiring miticide treatments would not be affected by loss of chlorobenzilate; i.e., $\Sigma_j \Delta A_j = \Sigma_k A_k$. The assumption is implicitly relaxed in the subsequent analysis that allows for price and quantity responses to whatever higher production costs a chlorobenzilate cancellation would occasion.

6. Our estimates of the acre-treatments for the chlorobenzilate mixtures are identical to those employed by OPP.

7. For part of the following analysis we accept OPP's assumption that the change in total acre-treatments for the alternatives will equal the present total acre-treatments with chlorobenzilate (i.e., $\Delta\Sigma_j A_j T_j = \Sigma_k A_k T_k$). However, we also investigate the implications of allowing differences in the treatment rates (T_j and T_k) to affect the acre-treatment estimates.

8. The anticipated change in acre-treatments for any one alternative is estimated through a two-step procedure. First, the acres treated with chlorobenzilate are divided among the alternatives in accordance with their current relative importance. That is, the increase in base acres treated with the jth alternative is estimated by

$$\Delta A_j = p_j \sum_k A_k ,$$

where p_j is the ratio of (1) base acres currently treated with the jth alternative to (2) base acres currently treated with all the relevant chlorobenzilate alternatives. We also investigate the implications of a maximum-plausible benefits assumption that loss of chlorobenzilate would lead to adoption of only the more expensive alternatives. (We explain this assumption more fully below.)

The second step in the procedure is to translate these acreage estimates into estimates of acre-treatments. For this task, we use the alternative assumptions mentioned above concerning the average number of treatments per year.

This procedure differs greatly from the approach employed by OPP (involving an equal division of acre-treatments among the alternatives). The implications of these different approaches to estimating the change in acre-treatments for the alternatives is illustrated in Table 7.14 for the case of Florida oranges. (See Appendix E for data on other use sites.)

9. The estimates of per acre material costs (*MC*) in the Doane miticide report appear to be unreliable (Luttner 1977a:48). Consequently, for chlorobenzilate and the major alternatives, we derive independent estimates of *MC* using information on product prices and application rates recommended in the state citrus guides.[5] For the various spray mixtures and a few of the alternatives, we accept the *MC* estimates used by OPP. Table 7.15 presents the estimates of *MC* per acre that are used in the subsequent analysis.

10. Since growers usually spray their citrus groves a number of times in a season, it seems reasonable to assume that any regulatory decision concerning chlorobenzilate would not affect the number of times growers sprayed their groves. That is, in connection with the chlorobenzilate analysis, application costs can be taken as fixed—an assumption generally followed by OPP.

The Committee's estimates of increased pest control costs yielded by the various assumptions discussed above are presented in Table 7.16, together with OPP's estimates of the same quantities. Depending upon the

TABLE 7.14 Estimates of Acre-Treatments of Chlorobenzilate Alternatives: Florida Oranges

		Allocations Based on Current Use Patterns			
(1) Alternative	(2) OPP's Estimate	(3) Estimate Using OPP's Treatment Rates		(4) Estimate Using Doane's Treatment Rates	
Dicofol	103,000	10,300	(2.0%)	8,300	(1.8%)
Ethion	103,000	32,400	(6.3%)	28,000	(6.1%)
Ethion/oil	103,000	127,200	(24.7%)	102,800	(21.9%)
Sulfur	103,000	319,300	(62.0%)	309,500	(65.8%)
Oil	103,000	25,800	(5.0%)	20,800	(4.4%)
Total	515,000	515,000	(100 %)	470,200	(100 %)

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the alternatives; columns (3) and (4) allocate the base acres in accordance with the current relative importance of the various alternatives.

Source: Derived from Luttner (1977a).

set of assumptions selected, we estimate the increase in pest control costs following loss of chlorobenzilate to be somewhere between $2.4 million and $9.2 million (the range represents a 90 percent confidence interval; see Appendix F). Even under the maximum-plausible benefits assumptions, our estimate of the control cost savings from chlorobenzilate falls far short of OPP's estimate of $57,629,000. The fundamental reason for the divergent estimates lies in the assumptions concerning scalicide treatments in Florida and bud-mite treatments in California (see Table 7.11).

ECONOMIC EVALUATION OF THE BENEFITS OF CHLOROBENZILATE

This section presents an appraisal of the combined effect of yield, quality, and pest control cost changes within the context of conventional benefit-cost analysis. That is, it attempts both to measure the extent to which the use of chlorobenzilate occasions "real" gains—i.e., enhances society's opportunities for production or consumption—and to assess the distribution of gains and losses (including those of a purely pecuniary nature). The availability of effective substitutes (in addition to other reasons outlined in preceding sections) argues against attributing significant yield and quality effects to the use of chlorobenzilate.

TABLE 7.15 Unit and Per-Acre Material Costs for Chlorobenzilate and Alternatives, by State

Miticide	Unit Cost	Per-Acre Material Costs, by State			
		Arizona	California	Florida	Texas
Chlorobenzilate 4E	\$ 15.60/gal	\$ 7.80	\$ 7.80	\$ 4.88	\$ 6.83
Chlorobenzilate mixtures[a]	—	—	—	\$ 4.18[b]	\$11.50[c]
Carbophenothion 4E	\$ 13.50/gal	—	—	—	\$ 8.78[d]
Dicofol 4MF	\$ 18.24/gal	\$11.40	—	\$13.68	—
Ethion 4E	\$ 11.44/gal	—	—	\$ 8.93	\$11.44
Oil 97 percent	\$ 1.02/gal	—	\$33.02[e]	\$ 7.65	—
Sulfur 95 percent	\$113/ton	\$ 4.95	—	\$ 2.83	—
Carbophenothion/oil	—	—	—	—	\$14.78[d]
Dicofol/oil	—	—	—	—	\$18.24
Dicofol/sulfur	—	—	—	\$16.50[f]	—
Ethion/oil	—	—	—	\$15.05[g]	\$15.81[d]
Ethion/sulfur	—	—	—	\$10.00[d]	—

[a] Average of the material cost for all of the mixtures.

[b] This cost applies to Florida oranges (170,000 acre-treatments at an average of \$4.18 per treatment); the cost for Florida grapefruit is \$6.71 per acre (32,000 acre-treatments).

[c] This estimate applies to Texas oranges (10,000 acre-treatments); the cost for Texas grapefruit is \$17.50 (16,000 acre-treatments). Doane reports estimates of acre-treatment costs for chlorobenzilate mixtures on Texas oranges that average to \$4.81, an unbelievably small figure since chlorobenzilate alone is estimated to cost \$6.83 per acre-treatment (Luttner 1977a). The Doane information on *grapefruit* suggests that these mixtures exceed the cost of chlorobenzilate alone by as much as 70 percent; thus, we estimate the cost of these mixtures on Texas oranges to about \$11.50 (\$6.83 × 1.7 = \$11.61).

[d] Estimates taken from EPA (Luttner 1977a, pp. 50-52).

[e] The price used for narrow-range type oil in California is \$1.27/gal (USDA 1977b).

[f] Estimated by summing the costs of dicofol and sulfur.

[g] Based on OPP's assumption that ethion will be applied with 6 gallons of oil (\$8.93 + \$6.10 = \$15.03).

Consequently, we need consider only the treatment-cost implications of chlorobenzilate use.

As suggested in Chapter 5, conventional benefit-cost analysis defines the benefit of continued chlorobenzilate use as the sum of (1) the value of productive resources saved due to its use and (2) the value of any additional output it allows. In technical terms, the correct measure of benefits is the sum of the changes in consumers' and producers' surpluses

TABLE 7.16 Alternative Estimates of Increases in Pest Control Costs Following Cancellation (in thousands of 1975 dollars)

State	Estimates Based upon OPP's Treatment Rate[a,b]	Estimates Based upon Doane's Treatment Rate[a,b]	Cost Under Maximum-Plausible Benefits Assumptions[b,c]	OPP's Estimate
Arizona				
Lemons	–$ 1	–$ 1	$ 7	$ 0
California				
Lemons	$ 130-$870	$130-$870	$ 870	$ 4,821
Florida-IPM				
Grapefruit	$ 0-$500	$ 0-$500	$ 500	$ 8,569
Lemons	$ 0-$20	$ 0-$20	$ 20	$ 397
Oranges	$ 0-$2,440	$ 0-$2,440	$ 2,440	$41,525
Florida-non-IPM				
Grapefruit	–$ 90	–$ 60	$ 1,200	$ 468
Lemons	$ 40	$ 20	$ 70	$ 34
Oranges	$1,050	$560	$ 5,360	$ 1,541

Texas				
Grapefruit	$ 20	$ 10	$ 240	$ 44
Oranges	$ 130	$ 90	$ 160	$ 230
Total[d]	$1,370-$5,070	$750-$4,450	$10,870 (9,200)[e]	$57,629

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[a] Allocation of base acres underlying these estimates is based upon current use patterns (see text).

[b] The non-IPM cost savings from reduced usage of chlorobenzilate is as follows: Arizona—$16,000; California—$41,000, Florida; grapefruit—$654,000, lemons—$34,000, oranges—$2,395,000; Texas: grapefruit—$417,000, oranges—$204,000.

[c] The maximum-plausible benefits assumptions are (1) 27,500 acres in California will require an additional oil treatment; (2) the IPM effect in Florida will be $26/per acre; and (3) only the more expensive alternatives will be used.

[d] Columns may not sum to total due to rounding.

[e] The number in parentheses is an estimate of the upper limit of the 90 percent confidence interval for total benefits from chlorobenzilate use on citrus. The sum of the individual maximum-plausible benefits estimates (equal to $10.9 million) overstates the upper limits of the confidence interval and is presented here only to permit a comparison with OPP's maximum-plausible benefits estimates of $57.6 million. The lower limit of the estimated confidence interval is $2.4 million. The procedure used in deriving this interval estimate is presented in Appendix F.

occasioned by the use of chlorobenzilate. In principle, measurement of these benefit components requires reliable estimates of (or reasonable assumptions about) market demand and supply functions (although, as we note below, the estimates of treatment-cost effects developed in the preceding section probably provide a close approximation to the theoretically correct measure of the benefits of chlorobenzilate). Likewise, an analysis of the distributional effects of chlorobenzilate use (e.g., price increases to consumers) requires some information about market supply and demand conditions.

Demand and Supply Elasticities

Numerous estimates of demand elasticities for different types of citrus and citrus products are available (George and King 1971, Riggan 1965, Tilley 1977, U.S. EPA/USDA 1978, Ward and Kilmer 1978). Unfortunately, the estimates vary considerably across studies. The demand elasticity estimates range from -0.68 to -4.98 for fresh Florida oranges, and from -0.71 to -3.06 for processed products made from Florida oranges (e.g., frozen concentrate), although most of these estimates fall between -0.7 and -2.0. The one available estimated demand elasticity for fresh Texas oranges exceeds -31.0. Estimates for fresh Florida and Texas grapefruits center around -4.0, although demand elasticities for all grapefruit (fresh and processed) center around -1.0. We were unable to obtain any demand elasticity estimates for lemons.

As a result of the obvious uncertainty about the actual magnitude of the price elasticities of demand for the various types of citrus and citrus products, the subsequent analysis evaluates (with two exceptions) the efficiency and distributional implications of chlorobenzilate use under the alternative assumptions that the price elasticities of demand equal either -0.7 or -2.5. The exceptions to this procedure are associated with evaluating impacts on Texas oranges (both fresh and processed) and Florida lemons. Texas orange growers account for about 2 percent of the total U.S. production, and Florida lemon growers provide for no more than 6 percent of the total lemon market. Producers supplying such relatively small portions of a market almost surely confront highly price-elastic demands for their product (recall that the estimated price elasticity of demand for fresh Texas oranges was around -31.0). Consequently, the analysis centering on Texas oranges and Florida lemons assumes that the price for those products is effectively demand-determined (that is, the price elasticity of demand is assumed to be infinite or, at least, very large).

Estimates of the price elasticity of supply for the various types of citrus are not, to our knowledge, available. However, previous studies of short-run supply elasticities for certain agricultural commodities (e.g., see Tomek and Robinson 1972) suggest that the short-run supply elasticity for citrus probably lies around 0.2 and almost surely does not exceed 0.5. The subsequent analysis uses two alternative values for the price elasticity of supply for each of the various types of citrus, namely, zero (the usual OPP assumption) and 0.5.

Analysis

In addition to the assumptions concerning demand and supply elasticities, a number of other important assumptions will be invoked in the benefit assessment in this section.

First, the demand and supply functions are assumed to be linear (strictly speaking, they need be linear only in the "neighborhood" of the equilibrium values for price and quantity). The assumption facilitates conversion of the elasticity measures into slope and intercept "estimates" for the demand and supply curves.

Second, it is assumed that the average of prices and quantities for the 1974–1975 and the 1975–1976 seasons are short-run equilibrium values. The actual price-quantity data used in the analysis are presented in Table 7.17.

Third, the increase in variable costs per unit of output for the industry (that is, the upward shift in the industry supply curve) is assumed to equal (ΔPC - initial industry output). For instance, in the case of fresh Florida oranges, unit costs are estimated to rise initially—under the maximum-plausible benefits assumptions—by about 4 cents per box following the loss of chlorobenzilate (i.e., $554,000 in higher pest control costs divided by 12,564,000 boxes of fresh oranges). The shift in the supply curve is assumed to leave the slope of the curve unchanged.

The results of the benefit assessment by type of citrus are reported in Tables 7.18–7.23. Table 7.24 presents estimates of the aggregate effects. These estimates are based upon the maximum-plausible benefits assumptions discussed in the preceding section. The corresponding OPP estimates are also reported to facilitate comparisons. Note that our estimates are substantially lower than OPP's; virtually the entire difference arises from our differing appraisals of the effect of disallowing chlorobenzilate on the cost of IPM.

The estimates in these tables that correspond to the zero-elasticity-of-supply case are identical to the estimated maximum-plausible increases in pest control costs following a loss of chlorobenzilate. A perfectly inelastic supply curve means that growers would (as indicated) absorb all

TABLE 7.17 Average Price and Quantity Data for Citrus over 1974-1975 and 1975-1976 Seasons

	Fresh		Processed	
State	Price (per box)	Quantity (boxes)	Price (per box)	Quantity (boxes)
Grapefruit				
Florida	$2.77	19,583,000	$0.76	27,267,000
Texas	$2.14	5,960,000	$0.75	3,040,000
Other	—	4,818,000	—	4,908,000
Total U.S.	—	30,361,000	—	35,215,000
Lemons				
Arizona	$4.39[a]	4,810,000		
California	$4.39[a]	18,800,000		
Other	—	1,790,000		
Total U.S.	—	.5,400,000		
Oranges				
Florida	$2.18	12,564,000	$1.66	164,689,000
Texas	$1.74	2,745,000	$1.18	2,575,000
Other	—	36,590,000	—	21,135,000
Total U.S.	—	51,899,000	—	188,399,000

[a] The price data are not specific to a state; it is assumed that Arizona and California prices are the same.

Source: For oranges and grapefruit, price data are from Ward and Kilmer (1978); quantity data are from Growers Administrative Committee (1977). For lemons, price data are from U.S. EPA/USDA (1978); quantity data are based on information in USDA (1977a) and the U.S. Department of Commerce (1978).

cost increases and continue supplying the same quantity that was provided before the cost increase. It is notable that allowing for some price responsiveness in supply hardly affects the estimate of net benefits from the use of chlorobenzilate. Thus, OPP's neglect of supply responses was a justifiable approximation for the purpose of estimating net aggregate benefits.

However, Tables 7.18–7.24 also reveal that demand and supply conditions have to be taken into account in estimating the *distributional* implications of a chlorobenzilate cancellation (or other action). If short-run citrus supply is responsive to changes in price and variable production costs, then disallowing chlorobenzilate would lead to slightly higher prices (around 1–4 cents per box in most cases) for citrus and a

TABLE 7.18 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Arizona and California Lemons

OPP Estimate: -$4,821,000

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
$E_d = -0.7$	$E_s = 0$	$E_s = 0.5$
Users	-$875,000	-$761,000
Nonusers	0	+ 241,000
Consumers	0	- 354,000
Net effect	-$875,000	-$874,000
$E_d = -2.5$		
Users	-$875,000	-$784,000
Nonusers	0	+ 52,000
Consumers	0	- 141,000
Net effect	-$875,000	-$873,000

Note: E_d is demand elasticity; E_s is supply elasticity.

slight decline in the quantity supplied (not only by users of chlorobenzilate, but by the entire industry). These changes have the effect of transferring some of the increased pest control costs from users of chlorobenzilate to consumers. In addition, the higher prices confer large windfall gains on the nonusers of chlorobenzilate, again at the consumers' expense. This transfer between consumers and nonusing growers is the predominant reason why the total losses (to consumers and users) reported in Tables 7.18–7.24 exceed the net effect of a chlorobenzilate cancellation.

Some additional suggestive evidence on the probable distributional effects of a chlorobenzilate cancellation is provided in Table 7.25, which presents information about size distribution of orange farms in California and Florida. If we assume that these data are roughly representative of citrus farms generally, it appears that much of the burden imposed on chlorobenzilate users would fall on the relatively large operations (i.e., those with more than 100 acres—a category for which average annual sales per farm exceed $300,000). Nearly three fourths of the burden on users is expected to fall on Florida orange growers, and the data in Table

TABLE 7.19 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Fresh Florida Oranges

OPP Estimate: −$3,057,500

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
$E_d = -0.7$	$E_s = 0$	$E_s = 0.5$
Users	−$554,000	−$406,000
Nonusers	0	+ 79,000
Consumers	0	− 226,000
Net effect	−$554,000	−$553,000
$E_d = -2.5$		
Users	−$554,000	−$496,000
Nonusers	0	+ 31,000
Consumers	0	− 88,000
Net effect	−$554,000	−$553,000

Note: E_d is demand elasticity; E_s is supply elasticity.

7.25 indicate that around 77 percent of those costs will be borne by the larger operations.

COMPARISON OF REGULATORY OPTIONS

The preceding sections of this chapter have presented detailed analyses of the risks and benefits associated with uses of chlorobenzilate. This section will summarize the principal findings of those analyses and will apply them to the assessment of the costs (forgone benefits) and the reduction in risk that can be anticipated from a number of regulatory options. As mentioned in the risk section of this chapter, five options are being considered. They are:

A. Continue registration of all uses.
B. Cancel all noncitrus uses.
C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions of registration to require protective clothing and respirators; cancel all other uses.
D. Cancel chlorobenzilate use on citrus to take effect after 5 years, and in the interim apply option C.
E. Cancel all uses.

TABLE 7.20 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Processed Florida Oranges

OPP Estimate: −$40,006,500

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
$E_d = -0.7$	$E_s = 0$	$E_s = 0.5$
Users	−$7,246,000	−$5,296,000
Nonusers	0	+ 1,030,000
Consumers	0	− 2,953,000
Net effect	−$7,246,000	−$7,219,000
$E_d = -2.5$		
Users	−$7,246,000	−$6,563,000
Nonusers	0	+ 339,000
Consumers	0	− 983,000
Net effect	−$7,246,000	−$7,207,000

Note: E_d is demand elasticity; E_s is supply elasticity.

TABLE 7.21 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Florida Lemons

OPP Estimate: −$432,000

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
$E_d = -\infty$	$E_s = 0$	$E_s = 0.5$
Users	−$95,000	−$94,000
Nonusers	0	0
Consumers	0	0
Net effect	−$95,000	−$94,000

Note: E_d is demand elasticity; E_s is supply elasticity.

TABLE 7.22 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Florida and Texas Grapefruit

OPP Estimate: −$9,081,000

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
	$E_s = 0$	$E_s = 0.5$
$E_d = -0.7$		
Users	−$1,942,000	−$1,401,000
Nonusers	0	+ 300,000
Consumers	0	− 835,000
Net effect	−$1,942,000	−$1,936,000
$E_d = -2.5$		
Users	−$1,942,000	−$1,724,000
Nonusers	0	+ 128,000
Consumers	0	− 334,000
Net effect	−$1,942,000	−$1,930,000

Note: E_d is demand elasticity; E_s is supply elasticity.

TABLE 7.23 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: Texas Oranges

OPP Estimate: −$230,000

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
	$E_s = 0$	$E_s = 0.5$
$E_d = -\infty$		
Users	−$160,000	−$159,000
Nonusers	0	0
Consumers	0	0
Net effect	−$160,000	−$159,000

Note: E_d is demand elasticity; E_s is supply elasticity.

TABLE 7.24 Alternative Estimates of Forgone Benefits Under Maximum-Plausible-Case Assumptions: All Citrus

OPP Estimate: −$57,629,000

Committee Estimates

Alternative Demand Conditions	Alternative Supply Conditions	
$E_d = -0.7$ or $-\infty$	$E_s = 0$	$E_s = 0.5$
Users	−$9,200,000	−$6,869,000
Nonusers	0	+ 1,397,000
Consumers	0	− 3,696,000
Net effect	−$9,200,000	−$9,168,000
$E_d = -2.5$ or $-\infty$		
Users	−$9,200,000	−$8,310,000
Nonusers	0	+ 465,000
Consumers	0	− 1,308,000
Net effect	−$9,200,000	−$9,153,000

Note: E_d is demand elasticity; E_s is supply elasticity.

TABLE 7.25 Farm Size Distribution: California and Florida Oranges

	Size Category			
	0.1-24.9 Acres	25-49.9 Acres	50-99.9 Acres	100 or More Acres
Percentage of total state orange production attributable to each category				
California	15.4	16.7	21.2	46.7
Florida	6.7	7.1	9.0	77.2
Average annual sales per farm				
California	$12,000	$40,500	$82,200	$305,200
Florida	$ 7,600	$20,700	$43,300	$336,000

Source: All estimates based on data from U.S. Department of Commerce (1978, p. 118).

These options are basically the same as those considered by OPP (see Chapter 6), although the Committee lists two fewer. (It should be noted, however, that the Committee's labeling of the options differs somewhat from OPP's. Thus, the Committee's Option B, for example, does not correspond to OPP's Option B.) The PD 3 for chlorobenzilate (U.S. EPA 1978a) discusses the possibility of cancelling chlorobenzilate use only in Arizona (OPP's Option F). However, the option was eventually dropped from consideration by OPP. Thus, the Committee has chosen not to treat this potential option separately from the option that would cancel the uses of chlorobenzilate in all states.

The PD 3 also lists as a regulatory option the prohibition of chlorobenzilate-treated citrus pulp as cattle feed (OPP's Option G). The selection of this option would amount to a *de facto* cancellation of chlorobenzilate use on citrus. Apparently, the profits from the continued sale of citrus pulp for cattle feed would more than offset the losses that would be incurred from (voluntary) withdrawal of chlorobenzilate (U.S. EPA 1978a). In addition, in Options C through G, the PD 3 discusses allowing the use of enclosed cabs in lieu of protective clothing and respirators when applying chlorobenzilate. Growers would find this option to be expensive since it would require substantial modifications to the existing fleet of tractors. The most likely response of growers would be to substitute other chemicals for chlorobenzilate, rather than incur the capital costs associated with this regulatory option (U.S. EPA 1978a). Accordingly, the Committee has not considered the prohibition of citrus pulp as cattle feed or the use of enclosed cabs during application separately from the option to cancel all uses of chlorobenzilate (the Committee's Option E).

The major consequences to be expected from these options are summarized in Table 7.26 and portrayed graphically in Figures 7.2 through 7.5. Because of the substantial uncertainties surrounding all the estimates, more than one value is presented in each cell of the table (see Appendix F). In the cost row the three numbers for each option (except Option B) show the range from the lowest cost that the Committee believes to be at all conceivable to the highest one. (Recall that for Option B—cancel noncitrus uses—OPP's estimate is used and therefore no range is shown.) The cost measures presented in Table 7.26 and Figures 7.2 through 7.5 represent estimates of the discounted present value of the future benefits from chlorobenzilate that would be forgone as a result of adopting a particular option. These present values were calculated under the assumptions that the remaining economic lifetime of chlorbenzilate is 10 years and that the appropriate discount rate is 7 percent (see Chapter 5 for further discussion).[6]

In the dose rows, the values are to be interpreted differently. The first number indicates the Committee's best judgment of the lifetime dose likely to be received by the relevant population group in the event of the indicated regulatory option. The second number is a worst-case or maximum-plausible exposure estimate, that is, the dose that the Committee believes might conceivably be attained over a lifetime but is highly unlikely to be exceeded. In every case, the recorded dose is the sum of the lifetime dose of chlorobenzilate plus the equivalent dose of dicofol—one of the most risky alternatives to chlorobenzilate and one that is expected to replace 2–10 percent of chlorobenzilate under certain regulations—that could be anticipated under the regulatory option shown.

As one moves across Table 7.26 from Option A to Option E, the costs, or value of forgone benefits, increase. The probable lifetime doses decrease for all population groups, or at least do not increase, as one moves from continuing registration to increasingly stringent regulations. But the maximum-plausible doses, it should be noted, actually increase for the Florida and U.S. populations as one moves from Option D to Option E. This averse behavior results from the increased use of dicofol as the use of chlorobenzilate is more and more closely restricted. Thus, while we do not *expect* that the lifetime dose received by the Florida population will be any greater under Option E than under Option D, we think that, because of the larger amount of dicofol whose use will be induced by Option E, the dose might be as much as 23 percent greater.

The same data that are in Table 7.26 are presented in Figures 7.2 through 7.5 in a form that is easier to assimilate. In addition, the figures show dashed horizontal lines introducing a relevant comparison compound, heptachlor. These lines are labeled "chlorobenzilate-equivalent of heptachlor" and are drawn at the mean lifetime dose of heptachlor estimated for the total U.S. population and (where relevant) the statistically calculated dose that the most highly exposed 1 percent of the U.S. population was receiving before heptachlor was suspended, translated into chlorobenzilate-equivalent doses using the CAI's of heptachlor and chlorobenzilate as described in Chapter 4. It should be noted that in order to keep the graphs reasonably simple, the uncertainty in the CAI's (see Figure 7.1) has not been represented. Ideally, they should be, as described in Chapter 6.

The Committee found two reports that estimated the intake of heptachlor by the average member of the U.S. population: one by Nisbet (1976) and the other by CAG (1977). (In fact, Nisbet's report was prepared specifically for CAG.) Hence, there are two sets of heptachlor values in the figures. Nisbet estimated that at the time of the heptachlor

TABLE 7.26 Equivalent Lifetime Doses and Discounted Costs for Five Options for Regulating Chlorobenzilate

Present value	Regulatory Options[a]				
	A	B	C	D	E
Cost ($ million)					
Minimum-plausible	0		1.9	5.1	16.8
Probable	0	1.4[b]	2.9	18.6	40.8
Maximum-plausible	0		3.9	32.1	64.8
Equivalent lifetime doses of chlorobenzilate[c] (m moles/kg)					
Citrus ground applicators (700)					
Probable	0.48	0.48	0.27	0.17	0.06
Maximum-plausible	0.72	0.72	0.60	0.38	0.34
Florida population (8×10^6)					
Probable	0.23×10^{-3}	0.23×10^{-3}	0.23×10^{-3}	0.19×10^{-3}	0.15×10^{-3}
Maximum-plausible	2.0×10^{-3}	2.0×10^{-3}	2.0×10^{-3}	1.3×10^{-3}	1.6×10^{-3}[d]

U.S. population (excluding Florida) (212×10^6)					
Probable	0.18×10^{-3}	0.18×10^{-3}	0.18×10^{-3}	0.11×10^{-3}	0.045×10^{-3}
Maximum-plausible	0.73×10^{-3}	0.69×10^{-3}	0.69×10^{-3}	0.50×10^{-3}	0.60×10^{-3}[d]

[a] Regulatory options:

A. Continue registration of all uses.
B. Cancel all noncitrus uses.
C. Continue registration of chlorobenzilate use on citrus and amend the terms and conditions of registration to require protective clothing and respirators; cancel all other uses.
D. Cancel chlorobenzilate use on citrus to take effect after 5 years, and in the interim apply Option C.
E. Cancel all uses.

[b] No range accompanies the probable cost estimate since the Committee adopted OPP's point estimate of the increase in annual pesticide costs on noncitrus crops if chlorobenzilate were cancelled.

[c] Probable estimates are the sum of lifetime doses of chlorobenzilate from Table 7.6 and chlorobenzilate equivalents of lifetime doses of dicofol from Table 7.8, under the various regulatory options. Maximum-plausible estimates are derived from the comparable maximum-plausible dose data in Tables 7.6 and 7.8 by the procedures described in Appendix F.

[d] See text for explanation of why these doses increase over the previous option.

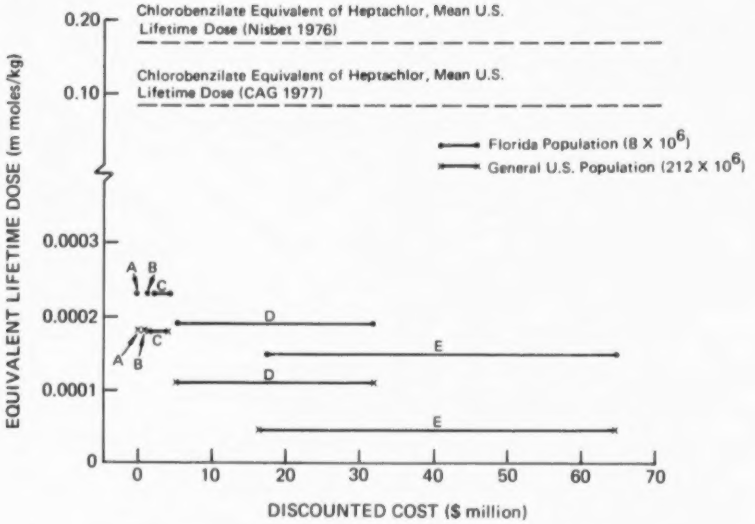

FIGURE 7.2 Equivalent *probable* lifetime doses for the *Florida* and *U.S. populations* and ranges of discounted costs under five options for regulating chlorobenzilate; heptachlor comparison shown (see text for discussion). Source: Table 7.26 and text.

suspension in 1975, the average member of the U.S. population was ingesting about 2.4 μg/day of heptachlor. At the time of the suspension, the limited economic lives of pesticides were not taken into account in estimating risk. Therefore, the Committee infers that the suspension was imposed in order to prevent the continuation of heptachlor intake over a typical lifetime of 70 years, an intake that would result in ingesting 0.00238 m moles heptachlor/kg of body weight/lifetime based on Nisbet's data. (The Administrator's order to suspend most heptachlor and chlordane uses was based on findings of widespread human exposure and the judgment, based on animal data, that the pesticides were carcinogenic. The imminent hazard posed by these findings was judged to outweigh the benefits of continued use.)

The CAI for heptachlor is 19.4 (see the section on Reference Compounds in this chapter), or 72 times that of chlorobenzilate (0.27, based on Innes *et al.* 1969), so that on the basis of Nisbet's data the dose of heptachlor that was being received at the time of its suspension is

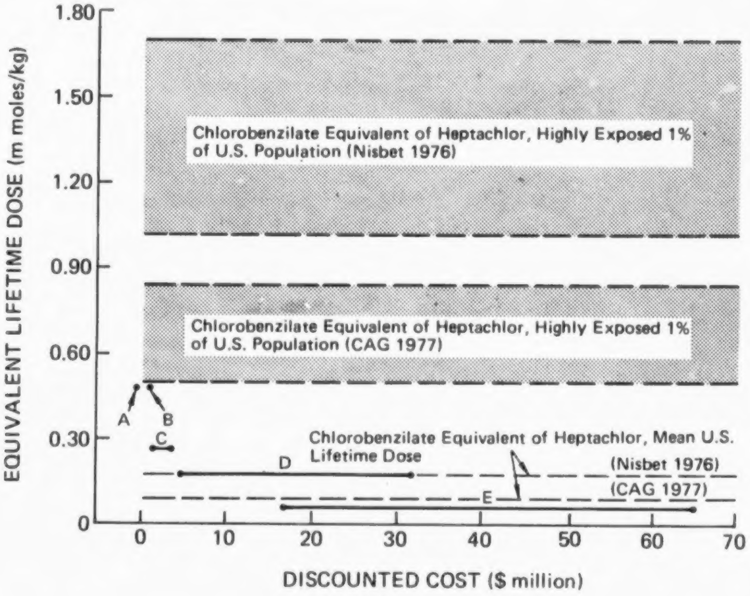

FIGURE 7.3 Equivalent *probable* lifetime doses for *citrus ground applicators* (700) and ranges of discounted costs under five options for regulating chlorobenzilate; heptachlor comparison shown (see text for discussion). Source: Table 7.26 and text.

equivalent to about 0.17 m moles chlorobenzilate/kg body weight as a probable lifetime exposure. Similarly CAG's value of 1.2 μg/day as the estimate of heptachlor ingested by the average member of the U.S. population is equivalent to about 0.084 m moles of chlorobenzilate/kg/lifetime. The most highly exposed 1 percent of the population was estimated by Nisbet to receive 6–10 times the mean daily exposure level. Therefore the Nisbet and CAG estimates are each multiplied by 6 and 10 to produce a range of estimates, shown in Figures 7.3 and 7.5, for the highly exposed groups. According to Nisbet, the highly exposed groups included children and breast-fed infants, freshwater fishermen and their families, and persons living near treated fields and in treated buildings. The mean cut-off equivalent dose of chlordane, the other comparison compound, is not shown; it is more than 3 times as great as the mean heptachlor dose being received by the general U.S. population

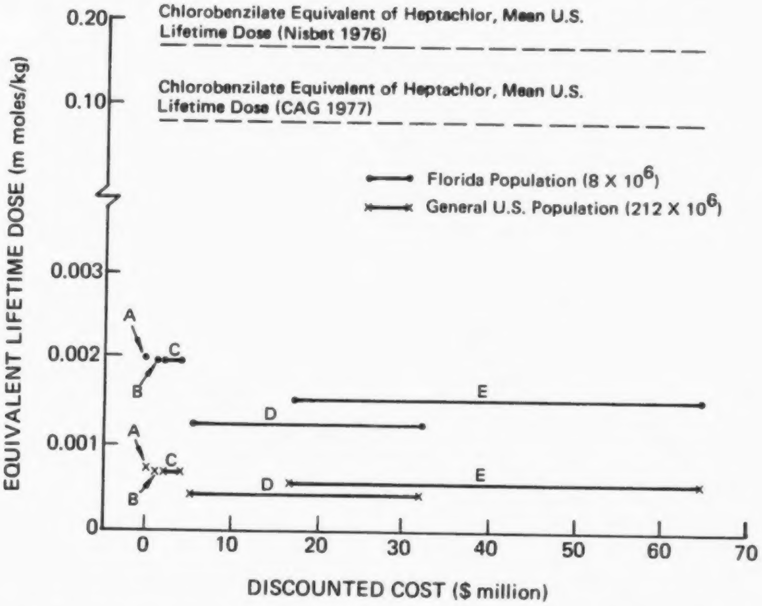

FIGURE 7.4 Equivalent *maximum-plausible* lifetime doses for the *Florida* and *U.S. populations* and ranges of discounted costs under five options for regulating chlorobenzilate; heptachlor comparison shown (see text for discussion). Source: Table 7.26 and text.

(based on an estimated lifetime exposure of 0.0081 m moles/kg [Nisbet 1976 and CAG 1977]). Recall that chlordane was also suspended and its major uses ultimately cancelled.

Figures 7.2 and 7.3 present probable lifetime doses of chlorobenzilate for each option, while Figures 7.4 and 7.5 show the maximum-plausible dose estimates. In each case, the first figure of the pair shows the general U.S. and the Florida populations while citrus applicators appear separately in the second. For the U.S. and Florida populations only the chlorobenzilate equivalents of the *mean* heptachlor dose are graphed. This is because chlorobenzilate doses under all five options are already below these values, making it unnecessary to add the higher chlorobenzilate-equivalent of heptachlor lines. For the citrus applicators, both the mean and high-exposure level chlorobenzilate-equivalent doses of hetptachlor are shown.

In the following discussion, the Committee has not attempted to

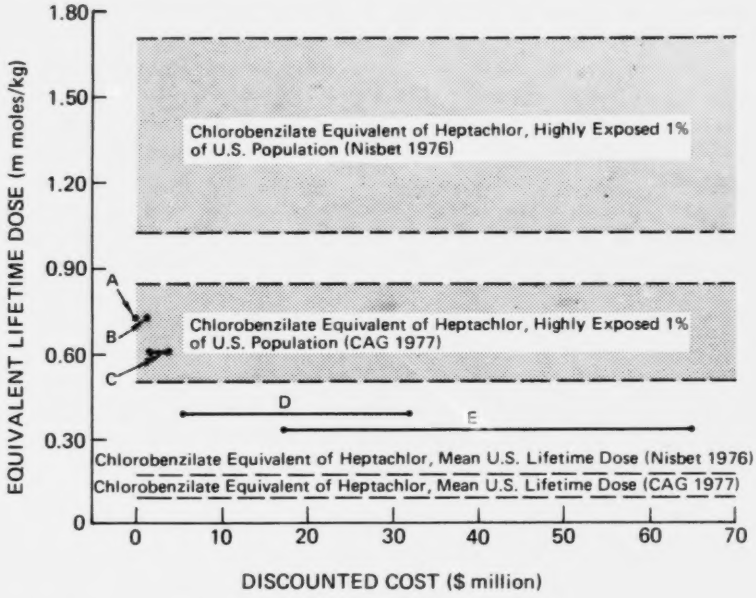

FIGURE 7.5 Equivalent *maximum-plausible* lifetime doses for *citrus ground applicators* (700) and ranges of discounted costs under five options for regulating chlorobenzilate; heptachlor comparison shown (see text for discussion). Source: Table 7.26 and text.

analyze similarities or differences in the size or compositions of the populations exposed to chlorobenzilate with those exposed to heptachlor. Such considerations may well be important. For example, is it more useful to compare a population of about 700 chlorobenzilate applicators to a population of 212 × 10^6 average Americans exposed to heptachlor or to a smaller population of breast-fed babies and young children receiving very high doses (from milk) for a short period of their life? This is a matter of judgment left to the Administrator. Furthermore, the economic impacts of the heptachlor suspension are not discussed. Although EPA did conduct an economic impact assessment (U.S. EPA 1976a), the decisions to suspend and ultimately cancel most heptachlor uses appear to have been based more on the risks involved than on the economic impacts, because alternative pesticides were predicted to be available and economic impacts were predicted to "be relatively minor in general and . . . (to) have no significant effect on production and prices of agricultural commodities, retail food prices, and otherwise on the agricultural economy" (U.S. EPA 1978c: 12375).

It is clear from Figure 7.2 that even without regulation, the intake of chlorobenzilate to which the U.S. population and Florida residents are exposed is orders of magnitude less than the equivalent intake of heptachlor corresponding to the mean levels at which its use was forbidden. The Committee recognizes that it is possible that heptachlor would have been suspended even if its dosage rate had been substantially smaller than the estimated levels. It is even possible that heptachlor would have been suspended at a dose level one thousandth as great as the estimated mean level being experienced at the time of the suspension in 1975, in which case its intake would be about equal to the intake of chlorobenzilate without regulation in terms of carcinogenic activity. That is a matter for the Administrator's judgment. The chart does make clear that the probable doses of chlorobenzilate received by food consumers are some 3 orders of magnitude below equivalent doses of heptachlor to which they had been exposed. The contrast is even greater for chlordane (not shown).

On the other hand, if we turn to Figure 7.3, it can be seen that citrus ground applicators are expected to receive nearly 4 times the mean chlorobenzilate equivalent of heptachlor cut-off for the general U.S. population under our Options A and B, about twice as much under Option C, a comparable amount under Option D, and about half as much under Option E. If, however, the probable chlorobenzilate doses to applicators are compared to the chlorobenzilate equivalent of heptachlor for the 1 percent of the U.S. population most highly exposed to heptachlor, all the options are expected to expose applicators to less than the high-level chlorobenzilate equivalent of heptachlor, although Options A and B are so close to the high-level cut-off based on CAG data, that they may be questionable.

The main implications of Figures 7.2 and 7.3 appear to be that Options A and B expose ground applicators to levels of risk that are nearly comparable to those being experienced by the populations that were highly exposed to heptachlor. Options D and E expose chlorobenzilate applicators to levels of risk roughly comparable to those that were experienced by the average member of the U.S. population in the heptachlor situation. Exposure of applicators under Option C falls in between. At the same time, the risks to the U.S. and Florida populations associated with the probable dietary exposures to chlorobenzilate appear to be too small to be at issue. It would obviously be useful to compare the doses of chlorobenzilate being received by the U.S. and Florida populations to chlorobenzilate equivalents of a previously regulated comparison compound that were lower than the current chlorobenzilate exposure levels. In the case of chlorobenzilate, our bank of reference compounds (Table 4.3) was insufficient to supply such a comparison.

We turn now to a consideration of the maximum-plausible dose levels of chlorobenzilate shown in Figures 7.4 and 7.5. Under all options, the highest doses that members of the U.S. population and Florida residents can plausibly be expected to receive by way of ingestion are of the order of 1 percent of the estimated chlorobenzilate-equivalent mean dose of heptachlor at the time that that pesticide was suspended (Figure 7.4). Citrus ground applicators, on the other hand, may plausibly be exposed to doses greater than the mean chlorobenzilate equivalent of heptachlor under any of the options (Figure 7.5). The excess is smallest under Option E, which requires immediate cancellation of chlorobenzilate use on citrus. Under Options A, B, and C, applicators may plausibly be exposed to doses comparable to the chlorobenzilate equivalent of heptachlor that the highly exposed members of the U.S. population were experiencing when heptachlor was cancelled. Options D and E may plausibly result in chlorobenzilate exposures to applicators that lie in between the mean chlorobenzilate-equivalent of heptachlor cut-off and the highly exposed.

Ultimately, the choice among options depends upon a judgment as to whether the indicated reductions in the doses received by ground applicators of chlorobenzilate are sufficient to justify the extra costs associated with adopting the more stringent regulations. The critical figures to review are Figures 7.3 and 7.5 pertaining to the probable and maximum-plausible chlorobenzilate exposures to citrus ground applicators together with the cost information along the *x*-axes. For example, looking at the move from Option C to Option D, it can be seen from Figure 7.3 that the cost of reducing the lifetime exposure of about 700 applicators by about 0.1 m moles/kg/person is expected to be about $16 million. Recall that this would place applicators at a risk roughly comparable to that being experienced by the average member of the U.S. population when heptachlor was cancelled. Similar comparisons of incremental costs with incremental reductions in exposure and the concomitant risk implications as one moves form one regulatory option to the next will provide the scientific basis for making decisions about regulating pesticides. It is interesting to note that had dicofol been submitted to RPAR together with chlorobenzilate, as would arise if the procedures recommended in Chapter 3 were adopted, the regulatory options would differ. For example, it is likely that they would include the option to cancel both chlorobenzilate and dicofol. This, in turn, might easily result in applicators' risks being reduced below those associated with the mean chlorobenzilate-equivalent of heptachlor cut-off. Of course, without having considered that option explicitly, it is difficult to predict what risks or costs from other substitute pesticides might enter the picture.)

NOTES

1. OPP assumes that about 19 percent of the chlorobenzilate acre-treatments would be replaced by dicofol (Luttner 1977a). However, as the benefit analysis in a subsequent portion of this chapter demonstrates, this assumption seems to have no factual basis and is not rigorously defended in the OPP benefit analysis. The range (2–10 percent) adopted by the Committee is admittedly arbitrary, but nevertheless is consistent with the treatment levels implied by current usage levels (see the Doane Specialty Crops Survey included in Luttner 1977a). Presently, dicofol accounts for only about 5 percent of the treatments on lemons and grapefruits and about 2 percent of the treatments on orange trees. In contrast, chlorobenzilate presently accounts for about 13 percent of the acre-treatments on lemons and about one third of the acre-treatments on oranges and grapefruits.

2. OPP estimates that cancellation of chlorobenzilate would increase annual pesticide costs on noncitrus crops by $194,000, with cotton accounting for $125,000 and fruits, nuts, and other crops accounting for the remaining $69,000 (U.S. EPA 1978a:67). The Committee does not question these estimates, largely because their magnitudes are so small relative to the estimated impacts on citrus growers and consumers.

3. The benefit assessment for chlorobenzilate was performed before the joint USDA/EPA assessment procedure was initiated. Therefore, the *Preliminary Benefit Analysis of Chlorobenzilate* (Luttner 1977a) was an EPA product to which the USDA reacted by producing a USDA assessment team report (USDA 1977b). EPA's supplement to the PBA (Luttner 1977b) responded to the USDA report.

4. The USDA assessment team was formed after OPP had completed the PBA (see note 2); consequently, information from the assessment team is used only in the *Supplement to the* PBA *of Chlorobenzilate* (Luttner 1977b).

5. Prices for chlorobenzilate, oil, sulfur, ethion, and dicofol (and various combinations of these miticides) were obtained from the USDA-ATR (USDA 1977b) and the Anderson-Muraro production budgets (Luttner 1977a). Whenever these two sources reported different prices for the same product, we used the average of the reported prices in our analysis.

6. The documented costs in Table 7.26 and Figures 7.2 through 7.5 are based upon the following estimates of annual forgone benefits (over a 10-year period). The noncitrus uses of chlorbenzilate are estimated to yield annual benefits of $194,000 (see note 2 to this chapter). The benefits from citrus uses range from $2.4 to $9.2 million annually, with the probable-case estimate being $5.8 million (see section on Changes in Pest Control Costs of this chapter for derivation of these estimates). Finally, the cost of providing applicators with protective clothing and respirators is assumed to be $100–$500 per applicator per year for a total annual cost of $70,000–$350,000. Neither OPP (U.S. EPA 1978a) nor the Committee developed actual empirical measures of the costs of protective clothing and respirators.

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APPENDIX A

Scientific Limitations to Extrapolating Data on Cancer Risk from Animals to Humans

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As noted in Chapter 4, CAG is directed by Agency guidelines (U.S. EPA 1976) to determine the carcinogenicity of chemicals and to provide numerical estimates of excess cancers in the human population that would result from current use of the compounds under scrutiny. The question of how—or even whether—to quantify human cancer risks has been the object of considerable controversy within both the scientific and federal regulatory communities for several years (Carter 1979). If relevant data were available, numerical estimates would contain less error, and less controversy would surround the issue. Few would doubt the scientific validity and precision of estimates of the human risk of cancer if the estimates were based on sound epidemiologic evidence, but such evidence is rarely available. Most commonly, only carcinogenicity test data derived from studies conducted with experimental animals are available and it is from such data that CAG generally determines whether and to what extent a compound appears to be a potential carcinogen to humans.

There is general agreement in the scientific community about a reasonable basis for qualitatively determining that a substance is a potential human carcinogen (IRLG 1979). The IRLG report, currently under review as federal guidelines to cancer risk assessment, provides a detailed consideration of this type of qualitative determination. The reader is referred to this source for additional information. The opinion is widely held that if a substance is demonstrated to be a carcinogen for any mammalian species in an appropriately designed and performed carcinogenesis bioassay, then the substance is likely to pose a potential cancer risk to humans (Upton 1979).

However, as we have noted, the qualitative evaluation is only half the charge given to CAG. They are also expected to estimate the impact of the carcinogenic compound in terms of quantitative tumor response in the human population by extrapolating from observed responses in animal test systems. It is this issue that is the source of so much debate. It is the opinion of the Committee that the current state of scientific knowledge does not permit meaningful and safe quantification of cancer risks in humans, and for that reason EPA's current practice should be abandoned or greatly modified. The error in EPA's risk estimates could be as much as 5 or 6 orders of magnitude, while benefit estimates can be trusted within 1 order of magnitude. (See Chapter 4.) The scientific considerations that lead us to this opinion are discussed briefly in this appendix.

SOURCES OF ERROR

Potential sources of error in making both qualitative and quantitative evaluations of carcinogenesis bioassay data are numerous. The determination that a chemical is carcinogenic rests upon demonstrating a statistically significant excess of tumors in experimental groups as compared to control groups. Inherent in this determination is an assessment of how adequately a study was performed, including the adequacy of the evaluation of the pathology of the tumors. Since the number of excess tumors ascertained will be used for determining quantitative risk, the ascertained and any error inherent in the evaluation propagated to yield the final error. Furthermore, in order to determine a meaningful excess incidence of tumors, statistical evaluation of tumor results must consider all the experimental and control animals, including premature deaths with or without tumors.

Next, the quantitative data from the bioassay must be extrapolated to conditions that apply to the induction of tumors in humans. There are several important differences to consider in comparing the conditions of experimental studies in animals and those of human exposure to presumed carcinogens. First, experimental studies are conducted in a species other than humans, most commonly rodents. Second, differences often exist between the route of administration of the carcinogenic compound to experimental animals and the typical route of exposure observed in human populations. Finally, practical considerations posed by the limited life spans of the experimental animals used in the studies and the limited sizes of experimental groups dictated by costs generally require that large doses of the compound be administered to the experimental animals. In contrast, estimated levels of exposure in the human population may be considerably smaller, often by several orders of magnitude.

Several other factors must also be considered, and any errors inherent in these processes quantified and included in the risk estimates. Such factors include the additive or synergistic effects of interactions between other carcinogens and the test compound in the human population, the biological and genetic diversity of the human population as compared to the experimental animals studied, and the effects of intercurrent disease in the human population. These factors would have to be combined with appropriate quantitative data concerning exposure to the compound in question within the human population.

PERFORMANCE OF CARCINOGENESIS BIOASSAYS

Before the recent effort to describe and adopt standard protocols, carcinogenesis bioassays varied widely in the manner in which they were performed. Factors such as the choice of experimental animal, the number of animals per experimental group, the dose of the test compound employed, the schedule for administering the compound, the conditions of housing and maintenance of the animals, and the duration of the experiment and procedure for terminating it (e.g., serial or terminal sacrifices, or lifetime holding) were all variables determined by the investigator. They frequently differed between individual investigators and even between individual studies by the same investigator. In the reports stemming from these studies, details of experimental technique are frequently omitted with the result that specific techniques are not definable. Frequently the chemical tested is not thoroughly evaluated in terms of purity and composition. Similarly, diets that were obtained from commercial sources may have changed in unknown respects between the interval in which the study was performed and the present. In cases where several chemicals were evaluated for carcinogenicity at the same time, it is rarely if ever evident whether animals exposed to more than one compound were held in the same room and in proximity to one another. It is also often unclear whether animals treated with known strong carcinogens as positive controls were housed together with the experimental animals.

Many of these uncertainties have been corrected or clarified in more recent studies, but the results of earlier investigations remain in the literature often without information vital to their thorough evaluation. When a compound is being considered for regulation, the early studies must be part of the evaluation. In its risk assessments, CAG is responsible for evaluating the results of every study available for a given compound and deciding whether and how to use them. CAG's assessment is subject to comment by all interested parties, any one of whom may challenge or attempt to revise CAG's evaluation of the adequacy of the relevant studies.

EVALUATION OF TUMOR PATHOLOGY

The basic data in a carcinogenesis bioassay are tumors observed in the experimental and control groups. The evaluation of the pathologic lesions in experimental and control animals of a bioassay is basically a subjective process. Morphologic lesions, both gross and microscopic, that may fall anywhere on a continuum of biologic diversity are assigned to discontinuous categories. The adequacy of the categorization depends on the insight into the morphologic manifestations of the natural history of the disease and the thoroughness with which individual categories are characterized and distinguished. Lesions may fall between clearly defined categories, and more than one type of lesion can occur concurrently in a given tissue. Furthermore, the natural histories of some disease processes in experimental animals are less well characterized than comparable lesions in humans. In such cases, it is more difficult to morphologically characterize and define lesions, and pathologists have less insight into the biological significance of the lesions. These factors influence the precision of categorization of pathology.

Diagnostic precision is also influenced by personal insights, skill, and experience. Although pathologic evaluations are admittedly subjective, rarely, if ever, is an attempt made to place a measure on the precision or accuracy of these diagnoses, that is, to determine precisely how the categorization or description of lesions characterize the pathology in that organism, or how well individual pathologists rate in their assignment of given lesions to appropriate categories. It is unclear in most cases whether this error is 20 percent, 10 percent, 5 percent, or 1 percent, and so on. As a consequence, the diagnoses are generally used as numerical data without error tolerances. Thus, a major potential source of error in the risk quantification never enters into a determination of error tolerances in the risk estimate.

The problem is compounded in older studies in which diagnostic material may be unavailable for subsequent reevaluation. Furthermore, diagnostic criteria and pathologic categorization may have changed during the interval between initial pathologic review and subsequent publication of a paper. For more recent studies, particularly those sponsored by the federal government, external review of pathologic evaluations has been instituted. This policy should presumably reduce error, but the extent of imprecision remains unclear.

EVALUATION OF RESULTS

Bioassay results may be evaluated according to incidence of tumors of all types within animal groups, incidences of tumors in specific locations, multiplicity of tumors, incidences of tumors of grouped organ sites, and so on. Methods for evaluating results vary both with the result observed and the procedures used for performing the bioassay. For example, different procedures may be used to evaluate studies in which whole animals survived to a terminal sacrifice as compared to studies in which excess early mortality occurred or animals were held until they died spontaneously. The availability of dose-response data provides additional bases for evaluating results. The difficulty involved in assessing excess tumors, therefore, varies with the results of a study.

In cases in which there is a large excess incidence of tumors in the test group, no comparable tumors in the control group, and both control and test groups are large, simple comparisons of the difference in tumor incidence may suffice. If the groups are not large, comparisons of tumor incidence must be supplemented with estimates of the imprecision of the experiment. Preferably, such error estimates should measure inherent inconsistencies or variances between studies in the effects of a given dose of a compound. Generally, however, there is only one test group in a study, or certainly only one group at a given dose level, making such estimates impossible. Thus, error estimates are generally based upon the size of the group used to make the comparison between test and control animals. When tumor responses are small or when there is a significant incidence of tumors in the control animals, the issue of experimental error becomes more critical, particularly when experimental groups are small and reliable estimates of biologic variability and response to the test compound are not available. For example, if, for a given site, tumors occur in the control animals, but a greater number of tumors is detected at this site in the one tested group, is this a real property of the test compound? Without knowing the variation of tumors in control animals at the given site, an excess of tumors in the test over the control group may only lie within the range of biologic variability of the test animals.

For studies in which animals are allowed to live until they die spontaneously, or studies that involve a terminal sacrifice but in which a large proportion die before termination, alternative methods for evaluating tumor responses are necessary. The general approach is an actuarial or life-table analysis. Specification of a defined end point in the study is critical to this approach. For example, the presence of a tumor that is uniformly lethal to the host is a defined end point. Similarly, tumors that are uniformly nonlethal and are found incidentally at death also present a defined end point. In contrast, tumors that may cause the death of an animal but do not necessarily do so, and may be found as incidental microscopic lesions, are less clearly defined as end points and pose difficulties in statistical analysis. Quantitative estimates of differences between control and test groups are difficult to make, and lack of precision here poses an even greater problem for quantification.

To summarize, the degree of difficulty in estimating excess tumor incidence relates in part to the magnitude of tumor excess in the test animals over the controls and in part to the number of premature deaths occurring in the test group as compared to the controls.

The preceding considerations apply to the qualitative determination of the carcinogenicity of a compound. All these factors also apply to the quantitative determination of the magnitude of carcinogenic response to a given mode of treatment with a test compound. In addition, as noted, several other factors must be considered in achieving a quantitative extrapolation to human cancer risks, and these factors are considered briefly below. Methods for determining human exposure have been considered in Chapter 4 and will not be reiterated here. It should be evident, however, that the error and imprecision inherent in estimates of human exposure must be propogated to yield the final estimate of tumor response in the human population and the error in the estimate offered.

EXTRAPOLATION TO LOW DOSES

Typically, constraints of time and money require that carcinogenesis bioassays be performed in rodents. Because of expense, control and experimental groups are limited generally to fewer than 100 animals and, frequently, to even fewer than 20. Consequently, to maximize the probability of detecting a positive tumor response, very high doses of test compounds are used. The doses are generally based upon the maximum tolerated dose that yields no excess subacute toxicity in the test group. Such doses are generally much higher than the typical dose to which humans are exposed—frequently by several orders of magnitude (on a milligram per kilogram body weight per lifetime basis).

The choice of these high doses is a pragmatic one, but it poses the problem of extrapolating from effects at high doses to tumor responses anticipated at the extremely low doses typical of human exposure. Since we do not have a comprehensive, detailed theory of carcinogenesis, we do not have a method for calculating the real number of tumors that will develop in experimental animals at a projected lower dose based upon observations at higher doses. However, numerous models have been proposed that make a variety of assumptions about the nature of carcinogenesis and offer a wide range of estimated tumor responses in a low-dose range. As has recently been reported for saccharin, depending upon which assumptions are made and consequently which extrapolation procedures are used, the errors in the predicted tumor incidence at low doses may range over 6 orders of magnitude in this case and could conceivably be higher in other circumstances (NRC/IOM 1978). Again, the estimates are based in science but rest on unproven assumptions, and the precision of the resulting estimates is unclear.

Because of the uncertainties inherent in extrapolation models, CAG generally uses the extrapolation that gives the highest reasonable estimate of cancer incidence within the dose range of human exposure. The linear nonthreshold model, although not likely to be close to reality for most compounds, is generally presumed to represent an upper bound on risk extrapolation in most cases. If, however, only one dose level is tested, and if the dose is in a saturation plateau of carcinogenic effect, then a linear nonthreshold extrapolation may underestimate the carcinogenic potential of the compound for a portion of the dose-response curve. Thus, under certain circumstances, even this rather "conservative" extrapolation procedure may provide an underestimate of effect. Nonetheless, the estimates are crude, and the extent of propagation of error in resulting human risk estimates is, again, unclear.

CORRECTION FOR DIFFERENT ROUTES OF ADMINISTRATION

Carcinogenesis bioassays are most typically performed by feeding the test compound to experimental animals. Less frequently, compounds are tested by application to the skin, by inhalation, or by subcutaneous or other routes of injection into the experimental animal. Although people are frequently exposed via ingestion, other routes of exposure may be important. Consequently, corrections must be made when the experimental route of exposure differs from the human. These corrections are generally not based on theory that is as well formulated as that on which the extrapolation from high to low doses is based.

The technique that CAG generally uses employs an analogy between the compound in question and a carcinogen that is chemically similar to the test compound and has been tested by a variety of routes. Short-term metabolic studies can indicate similarities or differences between the distribution of the comparison compound and the test compound and thus provide, by analogy, more insight into the validity of the comparison. The efficacy of tumor induction at various sites depending upon the route of administration can be determined for the comparison compound, and in this manner an analogy can be constructed. Unfortunately, there is a long history of peculiarities of individual chemicals; even chemicals that are structurally quite similar may manifest very different properties of distribution in the body and activation to carcinogenic forms. Thus, the precision of the comparisons is largely unmeasured.

Again, in practice, comparisons are generally made so as to maximize the estimated effect. Nonetheless, the estimates are crude and the extent of propagation of error in the resulting human risk estimate is unclear.

EXTRAPOLATION BETWEEN SPECIES

In making extrapolations between effects noted in rodents and those anticipated in humans, the extrapolator generally chooses the test species in which the largest tumor response per unit dose is observed. This is then considered the most sensitive test species, and it is generally assumed that the human population will be less sensitive. This assumption is largely based on the evaluation of six compounds for which quantitative exposure-tumor response data are available for both experimental animals and human populations. In these six cases, a reasonable comparability was determined between the extrapolated human tumor incidences and the animal dose-response data (NRC 1975). In each case where the most sensitive animal strain was selected, the anticipated or calculated human cancer risk was greater than that observed epidemiologically in the human population. However, such evidence for only six compounds does not prove the validity of the assumption, and there may indeed be compounds for which the extrapolation is not appropriate. For example, epidemiological studies indicated that benzene and arsenic are carcinogenic in humans, but experimental studies with these compounds have yet to prove conclusively that they are carcinogenic in animal bioassays. It is conceivable that in these two cases, the discrepancy arises from the fact that the human is the more sensitive species. Thus, in attempting to extrapolate between species, to make the assumption that the human is less sensitive than the most sensitive of the test species is not necessarily correct.

OTHER CONSIDERATIONS

Without a well-formulated, comprehensive theory and explanation for all or most facets of the development of human cancer, several critical determinants of risk in the human population may be omitted from the extrapolation procedures as currently performed. Factors *not now considered* include individual variability in the human population in response to exposure to carcinogens, effects of intercurrent diseases, and various forms of interactions between carcinogens, co-carcinogens, promoters, and other factors.

CAG PRACTICES

In determining whether or not a compound is a potential carcinogen, CAG is directed by the EPA guidelines to use a "weight-of-evidence" approach. The guidelines indicate the relative weight to be given to epidemiological studies, carcinogenesis bioassays, and short-term tests, but, as noted in Chapter 4, neither the guidelines nor CAG provide written criteria for following the approach. In fact there is uncertainty about how the approach is to be applied, particularly in cases where studies of the same type come to different conclusions regarding carcinogenicity or where the quality of studies compared differs substantially. It is unclear whether CAG adheres to a neutral or objective "weight-of-evidence" approach or whether it places greater weight on data suggesting carcinogenicity in an effort to avoid underestimating the potential for human cancer risk.

In making quantitative estimates, CAG's philosophy is to maximize each of the individual components employed in the extrapolation to estimate excess human cancer deaths, so that the real risk to which the human population may be subject will always be less than the estimated risk. This is a practical attempt to deal with the problem of limitations of current scientific knowledge. Since CAG recognizes that actual human risk is difficult or impossible to determine precisely, it attempts to estimate an upper bound of probable human risk. For each of the three extrapolations discussed above—high to low dose, test animal to human, and route of administration—CAG uses those assumptions and estimates that tend to maximize risk. Even human exposure estimates, not CAG's responsibility, are "upper-limit" estimates. The end result is that CAG propagates through the calculations those error tolerances that can be estimated, and the final estimate of excess human cancer incidence is reported as a range. The principal error arises in calculating the excess proportion of tumors occurring in the test group as compared to those arising in the control group and in correcting for the size of the experimental group, a factor that relates to the precision of the result. CAG results thus show an estimated number of excess cancer incidences with a range of confidence although, as noted above, all sources of error are not considered.

CAG informally urges caution in interpretation of its estimates. For example, if each of two estimates—say, 410 and 380 incidences—falls within the error tolerance of the other (the usual case), the two figures are not to be interpreted as significantly different. Nor are they to be interpreted as an actual excess of human cancer incidence of this precise magnitude. Instead, CAG's estimate is to be interpreted as an upper bound, and, presumably, the actual excess of human cancer incidence will be less than this number or less than the upper limit of the variability of this value. What CAG appears to believe is most important, however, is an extrapolated risk estimate (or better yet, its upper confidence limit) that falls below an incidence of one excess cancer; CAG tends to view this type of result as an indication that the compound in question is not a significant human cancer risk. But CAG's estimates would be more valuable if they were accompanied by these informal interpretations. Currently, the estimates stand as values with tolerance ranges that, contrary to the "warning-signal" stature recommended in the Agency guidelines, appear as actual numerical estimates of excess human cancer incidence attributable to use of the compound in question.

If CAG's risk estimates are to be used as intended two conditions must be met: (1) the estimates must be interpreted correctly by the Administrator, who is required to judge the balance between risks and benefits; and (2) the estimates must in fact be an upper bound on the real excess of human cancer incidence attributable to the compound. By presenting estimates of excess risk as numerical values, even with error tolerances, CAG provides values that appear to have tangibility and scientific validity. Although CAG members have attempted to provide Administrators with insight into the usefulness and limitations of the CAG estimates, it is difficult to judge how well they have succeeded. The estimates become a matter of record subject to evaluation and interpretation by individuals who do not have the benefit of CAG's informal interpretation of its own results. Thus, the presentation of the estimates without verbal explanation of how they might best be used exposes the figures to misinterpretation and misuse. In fact, the values are often erroneously accepted quite literally as sound scientific estimates with well-defined error limits.

The second point mentioned above concerns the adequacy of CAG estimates as an upper bound on real risk. As we have already seen, CAG has attempted to validate its extrapolation procedures on the basis of an NRC (1975) report that compares the results of animal studies and human epidemiologic investigations for six compounds—benzidine, chlornaphazine, DES, aflatoxin B_1, vinyl chloride, and cigarette smoking—for which dose-response data exist for both human exposure and animal experimentation. The NRC report concluded that, in at least four of the six cases, there is substantial agreement between the epidemiologically estimated excess of cancer deaths and the estimates extrapolated from animal studies. The translation of this limited conclusion, however, into a working hypothesis that human lifetime cancer incidence in general can be approximated by extrapolating from the lifetime incidence induced by similar exposure in laboratory animals is open to question. For example, CAG's estimates from human and animal data of the incremental risk per unit of inspired benzo(a)pyrene varied over 2½ orders of magnitude. One of the values determined from the animal studies was 2 orders of magnitude lower than that determined from epidemiological estimates, and another value was one twentieth of that estimated from the human studies (CAG 1978).

In addition to orders of magnitude disagreement between estimates from animal and human data, epidemiological estimates themselves are subject to error. These errors arise not only from imprecisions in the determination of excess cancers, but from difficulty in estimating actual human exposures. Epidemiological studies of vinyl chloride exposures and the related cancer risks are cited as a source of reliable dose-response data in the human population (NRC 1975). Yet, in this example, where efforts have been made to quantify exposure of the working population, the estimates are derived and not the product of precise measurement of doses. Exposures were estimated retrospectively on the basis of duration of employment and the specific job of individuals exposed during that period. The majority of the exposure estimates were derived from measurements of current levels of exposure to vinyl chloride in specific jobs, using current equipment and reagent stock. The extent to which these conditions apply to earlier periods of exposure is unknown. Furthermore, unlike the corresponding animal studies, the vinyl chloride workers were probably exposed to a combination of other organic materials that may influence the effects of the vinyl chloride (see below) (Nicholson *et al.* 1975). Consequently, even the case of vinyl chloride, considered by some a source of sound epidemiological dose-response data for excess cancer risk, is open to serious question concerning the precision of its exposure estimates. In most other epidemiological studies exposure estimates are less sound than in the case of vinyl chloride. Even in the case of human exposure to low doses of irradiation, where because of better dosimetry one might expect more precise estimates to be available than for chemical substances, expert opinions on estimated risks vary by 1–2 orders of magnitude (NRC 1979).

Furthermore, the six cases with "good" epidemiological data presented in the NRC report (1975) involved strong carcinogens. The majority of compounds that CAG will be required to assess will be weaker carcinogens than those noted above, and epidemiological evidence will generally not be available for validation of the extrapolated values. Therefore, even if one were to accept the validity of the epidemiological/experimental comparisons of the six tested compounds, one could not be sure that the relationship would still be valid for the more typical compounds CAG is asked to evaluate. Perhaps most distressing is that for some calculated incremental risks, benzo(a)pyrene for example, an estimate extrapolated from animal studies was not in fact an upper bound on the epidemiologically determined excess risk. One cannot be certain that the 2-order-of-magnitude discrepancy (underestimate) between one of the animal studies and the human epidemiological estimates will not be exceeded. This calls into question the fundamental premise that CAG estimates represent upper bounds on human cancer risk attributable to the use of a compound.

Thus, not only are there uncertainties in the evaluation of bioassay data, limitations in extrapolation methods, and omissions of factors in estimating risk because of lack of scientific knowledge, but CAG's assumption that their estimates are upper bounds can also be questioned. Within CAG these problems may be understood and recognized as part of the estimation process. Of greater concern, however, is the fact that once out of the hands of CAG, the estimates themselves are subject to misinterpretation.

CONCLUSIONS

The goal of quantifying assessments of human risk of cancer is attractive in theory. It could provide a comprehensible, quantitative measure against which to balance benefits and thereby make administrative decision making easier. It might also lead to some consistency among regulatory decisions, if the current attempt by federal agencies to agree on a uniform method of quantifying cancer risks is successful. Despite these advantages, the Committee concurs with this recent statement by Arthur Upton (1979), Director of NCI:

> Although an attractive idea, quantitative risk assessment involving extrapolation from animal data is not yet sufficiently developed to be used as a primary basis for regulating human exposure to carcinogens. Although we are correct in concluding *qualitatively* that animal carcinogens are potential human carcino-

gens, *quantitative* extrapolations involve potentially large errors, some of which could underestimate the actual human risk from exposure. Scientific knowledge is currently insufficient to lend precision to this process.

The attempt to precisely estimate quantitative cancer risks raises controversy because it requires scientific judgments and extrapolations which transcend the limits to our scientific knowledge. Important considerations have been omitted from estimates; this indicates they were either unrecognized (unlikely) or that no method was available for incorporating them. Furthermore, some of the factors integral to current quantification methods may have unquantified errors and thus be potential sources of further errors whose tolerances may be orders of magnitude in scale.

Substantial additional research is needed to add to current scientific knowledge before sound quantitative risk estimates can be achieved. Such research should focus on: mathematical modeling of carcinogenesis to learn more about dose extrapolations, synergistic and additive effects, and quantification of the precision and accuracy ranges of pathological evaluations. Support is also needed for development of sources of data and references for pathology, critical reviews of old carcinogenesis data, and development of a bank of well-characterized reference carcinogens with dose effects, pharmacodynamics, species differences, and other information.

The practical value of quantitative risk assessment alluded to above makes the pursuit of valid estimation a worthy goal. However, current methods need to be critically tested and scrutinized before they can become accepted procedure. Clear distinctions should be made between scientifically supportable components and those that are only best-guess extrapolations. The possibility of gross error, particularly underestimates, must be indicated. Overestimates involve the monetary costs of overregulating a compound; but underestimates are detected years later and are paid for in human deaths from cancer.

In closing, we repeat the theme of this appendix: until the scientific limitations to extrapolating numerical estimates of human cancer incidences from animal data are reduced, the Committee recommends that the practice be abandoned. EPA currently uses such estimates as a primary basis for regulating human exposure to carcinogens. Although Upton suggests that "regulatory decisions must be based on an evaluation of all the relevant information including the quantitative estimates of risk" (Upton and Nelson 1979), the Committee feels that until quantitative estimates are more sound, cessation of the quantitation of human cancer risk estimates appears to be the most certain method to prevent the misuse of such estimates. An alternative method for estimating risk is offered in Chapter 4 and applied in Chapter 7.

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APPENDIX B The Carcinogenic Activity Indicator

CAI's FROM ANIMAL DATA

A Carcinogenic Activity Indicator, as defined and used in this report, is:

$$\text{CAI} = \frac{\text{Excess percentage of subjects in which tumors are observed}}{\text{Lifetime dose (in m moles/kg of body weight)}} .$$

CAI's should be determined and expressed with confidence intervals derived from the experimental errors inherent in all the variables used in the calculation.

CAI's are not absolute estimates of the carcinogenic potency of compounds; rather they vary, depending upon the conditions or parameters that characterize the study from which they were derived. CAI values are basically intended to be used for comparisons between compounds. The more the study parameters characterizing CAI values for different compounds agree, the more likely it is that the CAI's can be validly compared.

Parameters that require specification include species of animal (and, for certain species, the strain within the species), route of administration, and approximate tumor excess level (this last to compensate for nonlinearities of dose-response curves). This list of parameters is not, however, necessarily sufficient. For example, sex may also be a determinant of the effectiveness of a substance in inducing cancer; in such cases it would also be an appropriate parameter. Also, CAI values may be calculated for a specific organ site or for all tumors. Ideally, CAI comparisons would be restricted to relative incidence rates at the same organ sites. If this is done, the organ site becomes another parameter of the CAI value; comparisons of CAI's for different compounds would have to consider whether the compounds are equally specific to the same target organ. In practice, however, the Committee feels that with appropriate caution aggregate totals of tumors also can be scientifically compared. As we better understand the process of carcinogenesis, additional parameters may require specification.

The excess percentage of subjects in which tumors are observed (in the numerator of the equation) is a measure of the proportion of the tumor response in the experimental group attributable to the test substance. Several considerations must be made in determining this value (see Appendix C). Allowance must be made for tumors in the control group. If the tumor incidence in the control group is excessively high, CAI calculations are highly constrained. In determining an error estimate, group sizes and the tumor incidence in the control group must be considered (e.g., with Abbott's correction, Abbott 1925). The forgoing presupposes that experiments are performed with nearly complete survival until a terminal sacrifice. In experiments where animals die spontaneously or where there has been excessive mortality prior to a terminal sacrifice, appropriate actuarial methods must be used to determine incidences of excess tumors.

The dose to which the tumor response is compared (the denominator of the equation) is in millimoles per kilogram of body weight integrated over the lifetime of the animal. The expression of the dose in this form is partially a matter of convenience and partially related to the compound chosen for illustration in this report, i.e., chlorobenzilate (see Chapter 7). The essential point is that the dose should be comparable between compounds, thus necessitating conversion to millimoles rather than grams or milligrams. To offer some basis for comparisons between species, the dose must be normalized to body weight of the animal. The total integrated dose over the lifetime of the animal was chosen in preference to dose rate (e.g., millimoles per kilogram per day) because of the discontinuous schedule of dosage in the most sensitive study of chlorobenzilate.

If dose is integrated over a lifetime, attention must be given to the dosing schedule: certainly equivalent doses given in the first and last 10 percent of an animal's lifetime would be expected to give different results. Similarly, single doses are likely to give results different from fractionated doses. Alternative CAI values could be constructed comparing substances on the basis of other measures of dose, e.g., millimoles per square meter of surface area per day. Again, when making comparisons of carcinogenic activity between compounds, it is most critical that appropriate judgment be given to selecting CAI values with comparable test parameters and reasonable biological similarities.

CAI's FOR HUMANS

In order to use the CAI comparisons derived from animal data to provide indications of the relative carcinogenic potential of the same compounds in humans, a number of assumptions must be invoked. The following four assumptions, for example, will justify statements about the relative dangers of two compounds, for convenience called pesticide *i* and pesticide *j*, in humans:

1. The ratio of CAI's in animals for pesticide *i* and pesticide *j* is the same at all levels of dosage (*D*).

Algebraically stated,

$$\frac{\mathrm{CAI}_a{}^i(D_1)}{\mathrm{CAI}_a{}^j(D_1)} = \frac{\mathrm{CAI}_a{}^i(D_2)}{\mathrm{CAI}_a{}^j(D_2)}$$

for all D_1 and D_2 greater than zero, where $\mathrm{CAI}_a{}^i(D)$ denotes the CAI for pesticide *i* in experimental animals at dose level *D*, and similarly for pesticide *j*. The assumption asserts nothing about the shapes of the individual dose-response curves, but it does state that they will be parallel if plotted on logarithmic scales.

2. For any dose level, *D*, the ratio of the CAI's that would be observed in experimental animals is the same as the ratio of the CAI's that would be observed in humans.

Algebraically,

$$\frac{\mathrm{CAI}_a{}^i(D)}{\mathrm{CAI}_a{}^j(D)} = \frac{\mathrm{CAI}_h{}^i(D)}{\mathrm{CAI}_h{}^j(D)}, \ D > 0.$$

The subscript *h* is introduced here to denote CAI values that pertain to humans. Algebraically, these two assumptions imply that

$$\frac{\mathrm{CAI}_h{}^i(D)}{\mathrm{CAI}_h{}^j(D)} = \frac{\mathrm{CAI}_a{}^i(D_a)}{\mathrm{CAI}_a{}^j(D_a)}, \ D > 0.$$

where D_o now denotes the observed experimental dose.

3. For low doses to which humans are typically exposed, the incidence of excess tumors induced by pesticides is in the same proportion as their CAI's.

Algebraically,

$$\frac{I_h{}^i(D)}{I_h{}^j(D)} = \frac{\mathrm{CAI}_h{}^i(D)}{\mathrm{CAI}_h{}^j(D)},$$

where D is a small positive dose level and $I_h^i(D)$ is the excess incidence of cancers induced in humans by dose D of pesticide i, and similarly for pesticide j.

4. For a restricted range of doses, the incidence of tumors induced in humans by a pesticide is proportional to the dose.

Algebraically,

$$\frac{I_h{}^i(D)}{I_h{}^i(D_1)} = \frac{D}{D_1}, \; r < \frac{D}{D_1} < \frac{1}{r},$$

where r is any number greater than zero.

Together, these four assumptions permit the calculation of equivalent doses from experimentally observed CAI's. By virtue of the first three assumptions, for any low dose, D_1, to which humans are typically exposed,

$$\frac{I_h{}^j(D_1)}{I_h{}^i(D_1)} = \frac{\mathrm{CAI}_a{}^j(D_o)}{\mathrm{CAI}_a{}^i(D_o)},$$

Invoking the last assumption,

$$I_h{}^j(D) = \frac{D}{D_1} \frac{\mathrm{CAI}_a{}^j(D_o)}{\mathrm{CAI}_a{}^i(D_o)} I_h{}^i(D_1),$$

provided that D/D_1 is not outside the designated range. Now choose D so that $I_h^j(D)$ is equal to $I_h^i(D_1)$. Then D is the dose of pesticide j that is equivalent to the prescribed dose D_1 of pesticide i and, cancelling,

$$\frac{D}{D_1} = \frac{\mathrm{CAI}_a{}^i(D_o)}{\mathrm{CAI}_a{}^j(D_o)}.$$

That is, the ratio of the equivalent doses of the two pesticides is the reciprocal of the ratio of their observed CAI's, provided the ratio so found is within the range for which the proportional response relationship is believed to hold.

None of these assumptions can be expected to apply precisely in practice. In fact we are not aware of any hard experimental evidence that supports them. Yet they, or assumptions of comparable strength, must be invoked whenever the results of bioassays are used to compare the potencies in humans of different compounds. The above assumptions appear to be plausible approximations for compounds whose chemical and biological properties are not excessively dissimilar. It is, perhaps, an indication of the poverty of our understanding that there is virtually no empirical evidence to indicate the circumstances under which these assumptions are or are not acceptable.

The assumptions described above have some theoretical implications. For example, it can be shown that assumption (1) is inconsistent with the popular "one-hit model," which implies the rather different potency index employed by Meselson and Russell (1977). There is no particular reason, aside from pedagogical convenience, for accepting the one-hit model. (For some empirical evidence on the validity of the one-hit model, see Ashley 1969.) The Committee therefore recommends the definition of the CAI that has been proposed above.

In view of the strong assumptions that have to be invoked, the CAI, like all other simple measures of carcinogenicity, must be interpreted with caution and discretion. Nevertheless, with the present state of our understanding, there is no scientifically warranted indicator of the hazards of being exposed to a carcinogen that can obviate the need for making assumptions as strong as these or stronger.

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APPENDIX C Estimates of the Carcinogenicity of Chlorobenzilate

EPA's CAG derived its estimate of the pathological activity of chlorobenzilate from observations by Innes (Anderson 1978:19, Innes *et al.* 1969). The data employed are reproduced in Table C.1. Applying Abbott's formula (see below) to these data, the excess probability of incurring a hepatoma among the test animals is found to be 0.476. Since this estimate was derived from a test group numbering only 17, it is subject to a substantial sampling error. In this appendix the 90 percent confidence interval for the excess probability of hepatomas will be derived and will be used to compute the 90 percent confidence interval for the CAI for chlorobenzilate.

TABLE C.1 Incidence of Hepatomas in Male Strain X Mice Given Chlorobenzilate (after Innes et al. 1969)

	Test Group	Pooled Control Group
With hepatomas	9	8
Without hepatomas	8	71
Group size	17	79

Source: Modified from Anderson (1978).

Let p_t and p_c be the proportions of test animals and control animals, respectively, that contracted hepatomas. Then Abbott's (Abbott 1925) formula for the excess probability of incidence among the test animals is:

$$p_x = 1 - \frac{1 - p_t}{1 - p_c}.$$

To a second-order approximation, the variance of p_x is then

$$\sigma^2(p_x) = \sigma^2\left(\frac{1 - p_t}{1 - t_c}\right)$$

$$= \left(\frac{1 - Ep_t}{1 - Ep_c}\right)^2 \left(\frac{\sigma^2(p_t)}{(1 - Ep_t)^2} + \frac{\sigma^2(p_c)}{(1 - Ep_c)^2}\right),$$

where σ^2 denotes variance and E is the expectation operator. The maximum likelihood estimates of the two variances are

$$s^2(p_t) = \frac{1}{17}\frac{9}{17}\frac{8}{17} = 0.01465,$$

$$s^2(p_c) = \frac{1}{79}\frac{8}{79}\frac{71}{79} = 0.00115.$$

Since the contribution of $\sigma^2(p_c)$ is relatively negligible, we neglect it, and assume $\sigma^2(p_c) = 0$. Then the variance formula reduces to

$$\sigma^2(p_x) \cong \frac{\sigma^2(p_t)}{(1 - Ep_c)^2} = \frac{\sigma^2(p_t)}{(1 - p_c)^2}.$$

Now

$$\sigma^2(p_t) = \frac{1}{\;} P_t(1 - P_t)$$

where P_t is the true, unknown, probability of hepatomas in a test animal. Applying Abbott's formula again,

$$P_t = p_c + (1 - p_c) P_x,$$

where P_x is the unknown excess probability of incidence in the test animals. When p_t and P_t are eliminated from these three equations,

$$\sigma^2(p_x) = \frac{1}{n}\frac{1 - P_x}{1 - p_c}(p_c + (1 - p_c) P_x).$$

The limits of the 90 percent confidence interval for P_x can now be computed. The sample size of 17 is large enough that the normal distribution is a satisfactory approximation to the binomial for all practical purposes. Then the upper limit of the confidence interval, denoted p_x, is the probability that satisfies

$$p - \alpha \sigma (p_x) = p_x$$

when P_x is replaced by p in the formula for $\sigma^2(p_x)$ and $\alpha = 1.6945$ is the normal deviate corresponding to a 5 percent tail. This equation can be written in the form

$$(p - p_x)^2 = \alpha^2 \sigma^2 (p_x) = \frac{\alpha^2}{n} \frac{1 - p}{1 - p_c} (p_c + (1 - p_c)p).$$

This is clearly a quadratic equation in p. Performing the indicated operations and rearranging produces the standard-form quadratic

$$\left(1 + \frac{\alpha^2}{n}\right)p^2 - \left(2p_x + \frac{1 - 2p_c}{1 - p_c} \frac{\alpha^2}{n}\right)p + \left(p_x^2 - \frac{p_c}{1 - p_c} \frac{\alpha^2}{n}\right) = 0,$$

in which $\alpha = 1.6945$, $n = 17$, and p_x is computed from Aboott's formula with $p_t = 9/17$ and $p_c = 8/79$. Making the numerical substitutions and solving the equation yields the two roots $p = 0.683, 0.260$. The larger root is the upper confidence limit that we sought. The smaller root is easily seen to be the lower confidence limit. Thus, the 90 percent confidence interval for P_x extends from 0.260 to 0.683.

The corresponding confidence interval for the CAI follows at once from the formula

$$\text{CAI} = \frac{100P_x}{\text{dose}},$$

where dose equals lifetime intake in millimoles per kilogram of body weight.

The calculation of the dose is as follows:

Daily ration	5 g
Concentration of chlorobenzilate	603 ppm
Daily intake of chlorobenzilate	3.015 mg
Duration of test	575 days
Total intake of chlorobenzilate	1733 mg
Molecular weight of chlorobenzilate	325.2
Total intake in m moles	5.33
Weight of animal	0.030 kg
Dose in m moles per kg per lifetime	178

The 90 percent confidence interval for the CAI therefore ranges from 0.146 to 0.384. The maximum likelihood estimate, which can be taken as the most-probable value, is $100p_z$ per dose = 0.267.

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APPENDIX

D Literature Search on the Biological Aspects of the Use of the Pesticide Dimethoate[1]

INTRODUCTION

Dimethoate is a systemic insecticide used extensively in agriculture. About 2 million lb are used annually in the United States, primarily on grapes, corn, cotton, sorghum, tobacco, alfalfa, safflower, and vegetable crops for controlling arthropod pests, such as sucking insects, leaf miners, and mites. The largest portion of dimethoate used on any single crop is on grapes, about 23 percent of production; beans account for another 11 percent of dimethoate used; and sorghum accounts for 16 percent. This appendix reports the results of a literature search concentrated on aspects of dimethoate use on pests of grapes in California (California produces about 90 percent of U.S. grapes). Data also are reported for beans and grain sorghum. Production, acreage harvested, value of harvest, and acreage treated with pesticides are given for these crops in Table D.1.

GRAPES

GRAPE LEAFHOPPER

Need for Grape Leafhopper Control

In California, the grape leafhopper, *Erythroneura elegantula*, is the single most important pest of grapes to be controlled with dimethoate. The

USDA/State assessment team on dimethoate cites leafhopper (including *E. variabilis*, a leafhopper pest of southern California) problems as being always heavy in the San Joaquin and Sacramento Valleys and in southern California. Losses due to uncontrolled leafhopper infestations in these areas are estimated at 50–100 percent; losses of 10–100 percent are estimated for other parts of California (USDA/State 1978).

According to Jensen *et al.* (1969), however, grapevines can tolerate high numbers of leafhoppers without reduction in yield or sugar content. The authors estimated that up to 20 leafhopper nymphs per leaf in the first brood and 10 nymphs in the second can be tolerated on Thompson Seedless grapevines. It was concluded that growers' tolerance of these levels of infestation would eliminate unnecessary pesticide applications and thereby reduce operating costs, retard the development of pesticide resistance by pests, and reduce incidences of biological disruption.

Lynn *et al.* (1965) found no differences in yield caused by leafhoppers between plots treated with insecticide and untreated plots. Apparently the leafhoppers were controlled by the parasitic wasp *Anagrus epos* (see below), after reaching a peak of eight nymphs per leaf in late July. The authors concluded that many grape growers use unnecessary pesticide treatments for leafhopper control, and that this practice sometimes results in severe secondary outbreaks of mite pests. Petersen (1965) is in agreement with this conclusion.

In much of California, primarily north and central California, grape leafhoppers are held below economic injury levels by the parasitic wasp *Anagrus epos*. This native wasp parasitizes leafhopper eggs, and overwinters on a noneconomic (i.e., one for which the cost of controlling exceeds the losses from not treating) leafhopper, the *Rubus* leafhopper, *Dikrella cruentata*. While the grape leafhopper undergoes reproductive diapause during the winter, the *Rubus* leafhopper remains active, living on evergreen *Rubus* species. Doutt and Nakata (1973) state that the peak spring emergence of *A. epos* adults from *Rubus* leafhopper eggs is simultaneous with the beginning of grape leafhopper oviposition in vineyards. At this time, *A. epos* expands its niche to include grape leafhopper eggs, and, where vineyards are near *Rubus* refuges, the proportion of grape leafhopper eggs killed is very high. If not disrupted by pesticide treatments, *A. epos* continues to heavily parasitize grape leafhopper eggs throughout the summer. In another paper, Doutt and Nakata (1965) state that the grape leafhopper/*Rubus* leafhopper/*A. epos* host-parasite complex occurs in the wild in California; and, where wild grapes and *Rubus* occur in the same area, there are no large populations of grape leafhoppers on wild grapes. Doutt *et al.* (1966) studied dispersal of *A. epos* from an artificial *Rubus* refuge and found that *A. epos*

TABLE D.1 Grape, Bean, and Sorghum Production and Pesticide Treatment in the United States

Crop	Acreage	Production (tons)	Value of Harvest	Percent of Acreage Treated		
				Insecticide	Fungicide	Herbicide
Grapes	—	4.005×10^{6a}	$\$619 \times 10^{6a}$	67^c	40^c	46^c
Beans	1.527×10^{6b}	$860{,}000^b$	$\$266 \times 10^{6a}$	70^c	24^c	65^c
Grain sorghum	14.88×10^{6a}	724×10^6	$\$1{,}486 \times 10^{6a}$	39^c	0^c	46^c

[a] Source: USDA (1977).

[b] Source: USDA (1977), dry edible beans only.

[c] Source: Pimentel et al. (1978).

effectively controlled grape leafhoppers for a radius of 3.5 miles around the refuge, an area of 38 square miles. However, Jensen *et al.* (1969) state that *A. epos* is not equally effective on all grape varieties and that planting *Rubus* refuges for overwintering *A. epos* populations is not always effective in controlling the grape leafhopper.

Toxicity of Dimethoate to Parasitoid Wasps

No data were found concerning dimethoate toxicity to *A. epos*. Bartlett (1963, 1966) reported that dimethoate is highly toxic to five species of parasitoid wasps, *Aphytis lignanensis*, *A. melinus*, *Metaphycis luteolus*, *M. helvolus*, *Spalangia drosophilae*, and *Leptomastix dactyloppii*. Shorey (1963) found dimethoate relatively nontoxic to the parasitic wasp *Diaretiella rapae*.

Effectiveness of Dimethoate for Leafhopper Control

AliNiazee *et al.* (1971) found dimethoate effective for leafhopper control on grapes at application rates of 1 lb/acre and 2 lb/acre. Jensen *et al.* (1961) found dimethoate effective for grape leafhopper control when 0.7 lb/acre was applied as dust or 1.1 lb/acre was applied in a water dilution, but not when 0.6 lb/acre was applied in a water dilution. Stafford and Kido (1969) found that dimethoate applied at 2 lb/acre reduced the leafhopper population by 99 percent on the test plot. No yield data were given in any of these studies.

PACIFIC SPIDER MITE

Need for Spider Mite Control

The most important mite pest of grapes in California is the pacific spider mite, *Tetranychus pacificus*. According to the USDA/State assessment team on dimethoate (USDA/State 1978), pacific mite populations increase rapidly during the warmer times of the year, and, within a 10-day period, an otherwise healthy vineyard may become brown and sickly because of mite feeding. Dimethoate gives adequate control, but is usually used only when leafhopper control is the primary objective. Mites are a problem in all grape-growing areas of California except the central coast, and are sporadically problematic in southern California.

Flaherty and Huffaker (1970) found no significant differences in yield between check plots and plots treated with acaricides when mite populations became large late in the growing season. However, a

TABLE D.2 Effects of Pacific Mites on Thompson Seedless Grape Berries and Raisins

	From Vines with Pacific Mite Damage	From Vines without Pacific Mite Damage
Average weight per berry (g)	1.96	2.02
Raisins (grade)[a]		
B+ (percent)	34	65
C (percent)	56	30
C− (percent)	10	5

[a] Raisin samples were run through the California Raisin Advisory Board Air Stream Sorter. B+ is above average heavy; C is minimum requirement; C− is not acceptable, too light. Sorter measures meatiness, which correlates with berry size and sugar content.

Source: Modified from Flaherty and Huffaker (1970).

decrease in berry size and quality was found when mite populations became large early in the season (Table D.2). Laing *et al.* (1972) studied the effects of pacific mites on grape yield and quality. Using a vine-by-vine analysis, the authors did not find significant correlation between mite densities on the grapevines and yield or sugar content of the grapes. The study was done in two vineyards. In the first, average mite density on vines sampled ranged from 2.1 to 225 mites/leaf during the 3-week study period; in the second, it ranged from 10.8 to 205.8 mites/leaf during a 4-week period. The authors concluded that high mite densities would have to occur early in the season to produce defoliation and a significant reduction in yield, but that late-season high mite densities may result in yield reductions in the following year. Kinn *et al.* (1974) also studied the effects of pacific mites on grape yield and quality and found that mite infestations caused reduction in grape quality only when the grapevines were under high stress. The authors report an increase in grape yield of 66 percent on plots where mite predators were released to control pacific mites.

Role of Mite Predator in Control of the Pacific Mite

The Phytoseiid mite, *Metaseiulus occidentalis*, is the most important native predator of pacific mites (Flaherty and Huffaker 1970, Kinn *et al.* 1974). Flaherty and Huffaker (1970) and Kinn and Doutt (1972) studied

M. occidentalis and pacific mites on grapevines. They found that in vineyards that were infrequently treated with pesticides, *M. occidentalis* was an efficient predator capable of controlling the pacific mite and able to respond to both high and low prey densities. The willamette mite, *Eotetranychus willamettei*, which was considered to be a serious pest in the past, was found to be relatively innocuous as a grapevine pest, and an integral part of the predator-prey system. The willamette mite is distributed diffusely on the grapevine in relatively stable numbers in contrast to the pacific mite, which congregates on leaves that receive the most sun and increases explosively in number during the warmer times of the year. In undisturbed vineyards, the willamette mite serves as a food base on which *M. occidentalis* maintains a stable population. Under these conditions, when the pacific mite starts to increase, *M. occidentalis* will be present in sufficient numbers to keep the pacific mite under control.

Secondary Mite Outbreaks

The pacific spider mite has become a serious pest of vineyards only since organic pesticides have come into widespread use for control of the grape leafhopper and other insect pests (Flaherty *et al.* 1969, 1972; Flaherty and Huffaker 1970; Kinn and Doutt 1972; Kinn *et al.* 1974; Laing *et al.* 1972). Furthermore, it has been noted that vineyards on which little or no pesticide has been used were not likely to have mite outbreaks, while those vineyards which relied on frequent pesticide use often had serious mite outbreaks (Flaherty and Huffaker 1970, Flaherty *et al.* 1972). Flaherty *et al.* noted that growers in Fresno County alone had been spending about $1 million annually on spider mite control, yet considerable vineyard damage still occurred.

Flaherty and Huffaker (1970) studied the vineyard mite situation in detail. They stated that pesticide treatments tend to disrupt the predator-prey balance by directly destroying the predators, or by indirectly destroying the predators by destroying their prey, or a combination of both. Once the predator population is destroyed, any surviving pacific mites can reproduce explosively and reach economically damaging densities before the predator population can increase enough to control them. This disruption leads to wildly fluctuating predator and prey populations and results in overexploitation of the prey by the predator, bringing about population crashes and continuation of imbalance. Once pesticide use is curtailed in a vineyard, it takes several years for a stable predator-prey balance to reestablish itself. Flaherty and Huffaker (1970) observed a 3-year average of 0.09 predator mites/prey mite during spring

TABLE D.3 Distribution of Peak Predator (*Metaseiulus occidentalis*) and Prey (Pacific and Willamette) Mite Populations in Pesticide Treated and Untreated Vineyards (last treated July, 1964; data collected August 19, 1970)

Item, Number of	Vineyard with Treatment History	Vineyard without Treatment History
Willamette mites on 40 leaves	9846	1500
Leaves (out of 40) with Willamette mites	40	27
Pacific mites on 40 leaves	3668	10
Leaves (out of 40) with Pacific mites	35	5
M. occidentalis on 40 leaves	67	29
Leaves (out of 40) with *M. occidentalis*	10	8
M. occidentalis to prey (ratio)	0.005	0.020

Source: Flaherty, D. L., and C. B. Huffaker. Biological control of Pacific mites and Willamette mites in San Joaquin valley vineyards. I. Role of *Metaseiulus occidentalis*. II. Influence of dispersion patterns of *Metaseiulus occidentalis*. Hilgardia 40:267-330, Copyright 1970. By permission of the University of California.

in a vineyard with a history of pesticide treatments, while one with no history of pesticide treatments had 2.42 predator mites/prey mite. More data are provided from these authors in Table D.3.

Flaherty and Huffaker (1970) suggested several measures that can help to restore mite predator-prey balance in vineyards once pesticide treatments have been stopped. It has been noted that vineyards planted with Sudan grass have less of a spider mite problem than the more common clean and cultivated vineyards. Sprinkler irrigation helps control mite pests without upsetting predators. Sprinkling costs more money than furrow irrigation, but the use of sprinkler irrigation increases grape quality and production, effectively reduces spring frost, summer heat, and powdery mildew problems, and saves money by reducing the need for pesticide applications. The judicious use of acaricides, which are selectively poisonous to pacific mites but not to *M. occidentalis*, can help the grower avoid loss during the normalizing period. Any practices that increase grapevine vigor reduce susceptibility to pacific mite damage.

Toxicity of Dimethoate to Phytoseiid Predators

No studies were found that tested the toxicity of dimethoate on *M. occidentalis*; however, data were found concerning other phytoseiids. Bartlett (1964), after studying the toxicity of pesticides on *Amblyseius* *hibisci*, concluded that low-persistence toxicants such as dimethoate can completely eliminate populations of phytoseiids. Bartlett found that dimethoate at 0.5 lb/acre was highly toxic to *A. hibisci*. Smith *et al.* (1963) studied the residual toxicity of 31 pesticides on *Typhlodromus fallacus* and *Phytoseiulus persimilis* and found that dimethoate residues remained toxic to these predators for 20 days, 7 days longer than any other pesticide tested. When 19 pesticides were tested for short-term toxicity, dimethoate was one of three pesticides that consistently cause 100 percent mortality in both predators. Watve and Lienk (1975) tested 36 pesticides for toxicity to *Amblyseius fallacis* and *Typhlodromus pyrii* and found dimethoate to be one of the two most toxic pesticides tested.

Effectiveness of Dimethoate for Pacific Mite Control

No usable data were found on the effectiveness of dimethoate for pacific mite control.

THRIPS

Western Flower Thrips

The western flower thrips, *Frankliniella occidentalis*, is attracted to grape flower clusters and may be present during fruit formation. The flower thrips cause scarring and dwarfing of new shoots in early spring. The flower thrips oviposit in developing berries, causing the formation of scars, called halo spots, which usually only mar the appearance of the grapes, but which can cause the skin of Italia grapes to weaken and break, leading to bunch rot (USDA/State 1978).

Jensen (1973) stated that only a few varieties of grapes, such as Almeria, Calmeria, and Italia, are ordinarily affected by halo spots. Yokoyama (1977b) studied scarring of table grapes by western flower thrips and found that the thrips scarred the rachis, laterals, and berry pedicels of Thompson Seedless and Calmeria grapes, but did not cause necrotic scars on the surface of the fruit. The author found that grape clusters that supported up to 1,582 thrips did not have a greater amount of surface scars than noninfested clusters. Data from Yokoyama are presented in Tables D.4 and D.5.

Jensen (1973) studied dimethoate for western flower thrips control and found that dimethoate-treated Calmeria and Italia grapes had significantly less halo spotting than untreated grapes, especially when treatment was applied during early bloom stages, or when multiple

TABLE D.4 Comparison of the Nymphal Populations and Fruit Quality of Thompson Seedless Grape Clusters That Were Protected from Natural Thrips Infestations (*Frankliniella occidentalis*) or Had Adult Thrips Caged on Clusters During Three Different Bloom Stages

		Number of Adults Introduced per Cluster			
Percent Bloom	Progeny and Cluster Quality	0	25	75	100
0	Number of nymphs	4 ± 2	326 ± 75	447 ± 200	887 ± 312
	Number of berries per centimeter of rachis	9 ± 3	11 ± 2	7 ± 3	10 ± 4
	Percent of berries with surface scars	6 ± 4	9 ± 3	21 ± 12	14 ± 5
50	Number of nymphs	[a]	257 ± 113	951 ± 101	927 ± 175
	Number of berries per centimeter of rachis	8 ± 2	14 ± 6	11 ± 4	13 ± 2
	Percent of berries with surface scars	11 ± 4	10 ± 5	8 ± 4	7 ± 2
100	Number of nymphs	[a]	606 ± 97	1035 ± 128	826 ± 464
	Number of berries per centimeter of rachis	10 ± 1	16 ± 3	10 ± 2	14 ± 8
	Percent of berries with surface scars	11 ± 7	4 ± 2	8 ± 6	9 ± 5

[a] This space is blank in the original paper.

Source: Modified from Yokoyama (1977b).

treatments were used (Tables D.6 and D.7). A paper by Jensen and Luvisi (1973) reported similar findings (Table D.8).

Grape Thrips

The USDA/State assessment team on dimethoate states that grape thrips, *Drepanothrips reuteri*, do most of their damage to grapes by scarring the berries and making them unfit for the table market. Grape thrips also damage the vines by feeding on the young leaves and tender shoots. Grape thrips are effectively controlled by dimethoate (USDA/State 1978).

Yokoyama (1977a) examined the effects of grape thrips on Thompson Seedless grapes and found that the thrips were not associated with scarred fruit. The thrips did cause distortion of some of the leaves, but the author concluded that it is unnecessary to control grape thrips as a routine vineyard practice.

BEANS

A summary of yield data found in the literature on dimethoate use on beans is presented in Table D.9.

GRAIN SORGHUM

The greenbug, *Schizaphis graminum*, is the most important sorghum pest controlled by dimethoate. The report of the USDA/State assessment team on dimethoate (USDA/State 1978) gave potential grain sorghum losses to greenbugs as 25 percent, if no controls were available to treat infestations.

Cate *et al.* (1973) carried out experiments to test the effectiveness of experimental and registered pesticides for greenbug control on grain sorghum. They found that yields were not increased by greenbug control at the levels of infestation encountered during the 3-year study, and concluded that much of the greenbug control practiced is unwarranted. DePew (1971) found that dimethoate treatment did not produce a statistically significant increase in grain sorghum yield. DePew (1972) and Daniels (1972) reported only small increases in yield due to dimethoate control of the greenbug (Table D.10).

Peters *et al.* (1975) and Teetes *et al.* (1975b) reported dimethoate resistance in strains of the greenbug. Grain sorghum strains have been developed that are effectively resistant to greenbug damage (Harvey and Hackerott 1974, Starks and Wood 1974, and Teetes *et al.* 1975a). Data from Harvey and Hackerott and Teetes *et al.* are given in Table D.11.

TABLE D.5 Comparison of the Quality of Calmeria Table Grapes That Were Exposed to *Frankliniella occidentalis* During Bloom

Percent Bloom	Number of Adults Caged per Cluster	Number of Berries per Centimeter of Rachis	Percent of Berries with Ovipositional Scars
0	0	2	0
50	0	6 ± 2	3 ± 3
100	0	8 ± 2	12 ± 22
100	25	5 ± 2	16 ± 8
100	75	7 ± 3	58 ± 3
100	100	5 ± 1	31 ± 22

Source: Yokoyama (1977b).

TABLE D.6 Effect of Dimethoate Treatment and Timing of Treatment on Thrips Damage to Italia Grapes (1 lb/acre dimethoate per treatment)

Treatment Dates	Percent Fruit with Halo Spotting
Check (no treatment)	18.3
May 1 (5 percent bloom)	4.02
May 8 (95 percent bloom)	4.37
May 15 (shatter stage, berries 4-5 mm in diameter)	14.4
May 22	17.9
May 1, 8, 15, 22	0.559

Source: Adapted from F. Jensen. Flower thrips damage to table grapes in San Joaquin Valley: (1) Halo spot timing; (2) nymphs and scarring. *California Agriculture* 27(10):6-7, Copyright 1973. By permission of the University of California.

TABLE D.7 Effect of Dimethoate Treatment and Timing of Treatment on Thrips Damage to Calmeria Grapes (1 lb/acre dimethoate per treatment)

Treatment Dates	Percent Fruit with Halo Spotting
Check (no treatment)	12.6
May 8 (20 percent bloom)	7.24
May 15 (70 percent bloom)	3.42
May 22 (past shatter, berries 4-6 mm in diameter)	9.15
May 30 (berries 6-8 mm in diameter)	13.4
May 8, 15, 22, 30	0.652

Source: Adapted from F. Jensen. Flower thrips damage to table grapes in San Joaquin Valley: (1) Halo spot timing; (2) nymphs and scarring. *California Agriculture* 27(10):6-7, Copyright 1973. By permission of the University of California.

TABLE D.8 Effect of Dimethoate Treatments and Timing of Treatments on the Amount of Halo Spotting of Thompson Seedless Grapes (1 lb/acre dimethoate per treatment)

Date Treated	Area of Berry Scarred[a]
Checked (no treatment)	5.11
April 29 (early bloom)	1.19
May 9 (100 percent plus bloom)	0.794
April 29 and May 9	0.394

[a] The area of berry scarred is the product of the percentage of berries in a cluster with scars, times the percentage of the surface covered by the scarring on the affected berries, divided by 100.

Source: Modified from F. Jensen and D. Luvisi. Flower thrips nymphs involved in scarring of Thompson seedless grapes. *California Agriculture* 27(10):8-9, Copyright 1973. By permission of the University of California.

TABLE D.9 Effect of Dimethoate Treatment to Control Various Arthropod Pests on Beans

State	Crop	Treatment	Yield	Data Source
Leaf Hopper Control				
Maryland	Snap beans	Check	23.8 lb/plot	Ratcliffe et al. (1960)
		0.25 lb/acre spray	25.6 lb/plot	
		0.50 lb/acre spray	24.8 lb/plot	
		1.00 lb/acre spray	26.9 lb/plot	
Florida	Bush beans	Check	45.6 oz/100-ft row	Wolfenbarger (1963)
		1 pt/100 gals spray	96.1 oz/100-ft row	
Corn Earworm Control				
Maryland	Lima beans	Check	1.4 lb/plot	Ratcliffe et al. (1960)
		1.0 lb/acre spray	7.0 lb/plot	
Mites and Lygus Bug Control				
Washington	Field beans	Check	2506 lb/acre	Hagel (1970)
		2 lb/acre spray	2198 lb/acre	
Lygus Bug Control				
California	Lima beans	Check	963 kg/ha	Bushing and Burton (1974)
		early season 0.56 kg/ha spray	2866 hg/ha	
		midseason 0.78 kg/ha spray		
California	Lima beans	Check	20 beans/plant	Shorey et al. (1965)
		1 lb/acre spray	36 beans/plant	
Thrips Control				
Georgia	Lima beans	Check	4749	Dupree (1970)
		1 lb/acre soil banded	4070	
		Check	4059 lb/acre	
		1 lb/acre soil banded	4193 lb/acre	

TABLE D.10 Effect of Dimethoate Treatments for Greenbug Control on Grain Sorghum

State	Treatment	Yield	Source
Kansas	Check	4754 lb/acre	DePew (1972)
	0.25 lb/acre spray	4879 lb/acre	
Texas	Check	1461 lb/acre	Daniels (1972)
	0.15 lb/acre spray	1461 lb/acre	
	0.50 lb/acre spray	1559 lb/acre	

TABLE D.11 Grain Sorghum Yield of Greenbug Susceptible and Resistant Strains of Sorghum

Sorghum Strain[a]	Greenbug Exposure	Yield	Source
Susceptible	Yes	158 g/plant	Harvey and Hackerott (1974)
Susceptible	No	211 g/plant	
Resistant	Yes	186 g/plant	
Resistant	No	179 g/plant	
Susceptible X Resistant	Yes	179 g/plant	
Susceptible X Resistant	No	190 g/plant	
Susceptible X Susceptible	Yes	2600 lb/acre	Teetes et al. (1975a)
Susceptible X Resistant A	Yes	5500 lb/acre	
Susceptible X Resistant B	Yes	4317 lb/acre	
Resistant C X Resistant A	Yes	4233 lb/acre	

[a] The use of an X in this column indicates a cross between strains with the resultant progeny used in the experiment.

NOTE

1. None of the literature cited in this appendix was referenced in the draft report of the USDA/State assessment team on dimethoate (USDA/State 1978) submitted to EPA as input into the economic impact analysis for the dimethoate RPAR. As of this writing, the final report of the USDA/State assessment team was not complete. However, the sections on grapes, beans, and sorghum were not expected to vary from the draft version.

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APPENDIX E Estimates of Acre-Treatments for Chlorobenzilate Substitutes

The information in this Appendix supplements Table 7.14 in Chapter 7. For an explanation of the appendix tables see the section on An Economic Evaluation of the Benefits, subsection on Changes in Pest Control Costs in Chapter 7.

REFERENCE

Luttner, M.A. (1977) Preliminary Benefit Analysis of Chlorobenzilate. Benefit and Field Studies Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. (Unpublished)

TABLE E.1 Estimates of Acre-Treatments for Chlorobenzilate Substitutes: Arizona Lemons

		Allocations Based on Current Use Patterns	
(1) Substitute	(2) OPP's Estimate	(3) Estimates Using OPP's Treatment Rates	(4) Estimates Using Doane's Treatment Rates
Dicofol	666	800	800
Sulfur	666	1200	1200
Ethion	666	0	0
Total	2000[a]	2000	2000

[a] Column does not sum to total due to rounding error.

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the substitutes; columns (3) and (4) allocate the base acres in accordance with current relative importance of the various substitutes.
Source: Derived from Doane Specialty Crops Studies 1972, 1973, and 1974 (reported in Luttner (1977)), Luttner (1977), and Tables 7.12 and 7.13 of this report.

TABLE E.2 Estimates of Acre-Treatments for Chlorobenzilate Substitutes: Florida Grapefruit

		Allocations Based on Current Use Patterns	
(1) Substitute	(2) OPP's Estimate	(3) Estimates Using OPP's Treatment Rates	(4) Estimates Using Doane's Treatment Rates
Dicofol	17,429	2,000	1,300
Ethion	17,429	5,700	4,500
Oil	17,429	0	0
Sulfur	17,429	86,700	86,700
Dicofol/sulfur	17,429	1,200	1,200
Ethion/oil	17,429	25,700	17,500
Ethion/sulfur	17,429	1,200	1,200
Total	122,000	122,500	112,400

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the substitutes; columns (3) and (4) allocate the base acres in accordance with current relative importance of the various substitutes.
Source: Derived from Doane Specialty Crops Studies 1972, 1973, and 1974 (reported in Luttner (1977)), Luttner (1977), and Tables 7.12 and 7.13 of this report.

TABLE E.3 Estimates of Acre-Treatments for Chlorobenzilate Substitutes: Florida Lemons

		Allocations Based on Current Use Patterns	
(1) Substitute	(2) OPP's Estimate	(3) Estimates Using OPP's Treatment Rates	(4) Estimates Using Doane's Treatment Rates
Dicofol	1,400	2,300	1,600
Ethion	1,400	0	0
Oil	1,400	0	0
Sulfur	1,400	2,300	2,300
Ethion/oil	1,400	2,300	1,600
Total	7,000	6,900	5,500

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the substitutes; columns (3) and (4) allocate the base acres in accordance with current relative importance of the various substitutes.
Source: Derived from Doane Specialty Crops Studies 1972, 1973, and 1974 (reported in Luttner (1977)), Luttner (1977), and Tables 7.12 and 7.13 of this report.

TABLE E.4 Estimates of Acre-Treatments for Chlorobenzilate Substitutes: Texas Grapefruit

		Allocations Based on Current Use Patterns	
(1) Substitute	(2) OPP's Estimate	(3) Estimates Using OPP's Treatment Rates	(4) Estimates Using Doane's Treatment Rates
Carbophenothion	7,200	16,000	15,200
Ethion	7,200	2,000	3,000
Dicofol/oil	7,200	1,800	2,700
Carbophenothion/oil	7,200	13,000	10,400
Ethion/oil	7,200	3,000	3,500
Total	36,000	35,800	34,800

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the substitutes; columns (3) and (4) allocate the base acres in accordance with current relative importance of the various substitutes.
Source: Derived from Doane Specialty Crops Studies 1972, 1973, and 1974 (reported in Luttner (1977)), Luttner (1977), and Tables 7.12 and 7.13 of this report.

TABLE E.5 Estimates of Acre-Treatments for Chlorobenzilate Substitutes: Texas Oranges

		Allocations Based on Current Use Patterns	
(1) Substitute	(2) OPP's Estimate	(3) Estimates Using OPP's Treatment Rates	(4) Estimates Using Doane's Treatment Rates
Carbophenothion	3,286	1,500	1,400
Dicofol	3,286	0	0
Ethion	3,286	0	0
Propargite	3,286	0	0
Fenbutatin-oxide	3,286	0	0
Ethion/oil	3,286	4,600	5,300
Carbophenothion/ oil	3,286	16,900	13,500
Total	23,000	23,000	20,200

Note: Column (2) assumes an equal allocation of chlorobenzilate's base acres among the substitutes; columns (3) and (4) allocate the base acres in accordance with current relative importance of the various substitutes.

Source: Derived from Doane Specialty Crops Studies 1972, 1973, and 1974 (reported in Luttner 1977), Luttner (1977)), and Tables 7.12 and 7.13 of this report.

APPENDIX

F Construction of Confidence Intervals for Mathematical Combinations of Random Variables

Many of the variables central to risk and benefit analyses will generally be measured with imprecision. Accordingly, the Committee has recommended in this report that the estimates for such variables be reported as 90 percent confidence intervals rather than as single point estimates. (Of course, inadequacies with the data will require most of the ranges to be subjectively determined, on the basis of the analyst's judgment.)

In such instances, variables are estimated by mathematically combining (e.g., adding, multiplying) estimates of other variables. For instance, total benefits forgone due to the withdrawal of chlorobenzilate are measured by the sum of benefits forgone from the citrus and noncitrus uses. If the mathematical manipulations involve two or more variables measured as intervals, caution must be exercised in forming the confidence interval for the derived estimate. This appendix presents the correct procedure for combining estimates of random variables to derive estimates of and confidence intervals for other random variables.[1]

The following discussion is framed largely in terms of the two-variable case. The randomly distributed variables are denoted by x and y. Further, their expected values and variances are denoted by $E(x)$ and $E(y)$ and by $V(x)$ and $V(y)$, respectively. The covariance between x and y is denoted by $C(x, y)$.

SUMS AND DIFFERENCES OF RANDOM VARIABLES

If the variables x and y are to be combined to form a new variable $z = x \pm y$, then $E(z) = E(x \pm y) = E(x) \pm E(y)$. Thus, the best estimate of z is simply the sum (or difference) of the best estimates of x and y.

The variance of z is $V(z) = V(x) + V(y) \pm 2C(x, y)$. Clearly, if the variables are independently distributed, the variance of their sum or difference is simply the sum of their variances: $V(x) + V(y)$. These results easily generalize to the case involving three or more random variables (see Mood *et al.* 1974).

PRODUCT OF RANDOM VARIABLES

Suppose that x and y are to be combined to form a product, $z = xy$. In this case, $E(z) = E(xy) = E(x)E(y) + C(x, y)$. Of course, if x and y are uncorrelated, then $E(z) = E(x)E(y)$.

The variance of the product of two random variables assumes a rather complex form when x and y are correlated. In general, the data available to OPP would not permit the use of this formula, so it is not shown here. (The interested reader may refer to Mood *et al.* 1974.) If x and y are independently distributed, the variance of the product is relatively straightforward:

$$V(xy) = E(x)^2V(y) + E(y)^2V(x) + V(x)V(y).$$

These results also generalize to cases involving three or more variables (Goodman 1960).

QUOTIENT OF TWO RANDOM VARIABLES

In general, there are no simple exact formulas for the mean and variance of the quotient of two random variables, although there are some approximate formulas (Mood *et al.* 1974). The formulas used by the Committee are

$$E\left(\frac{x}{y}\right) \cong \frac{E(x)}{E(y)} - \frac{C(x, y)}{E(y)^2} + \frac{E(x)V(y)}{E(y)^3},$$

and

$$V\left(\frac{x}{y}\right) \cong \left(\frac{E(x)}{E(y)}\right)^2 \left(\frac{V(x)}{E(x)^2} + \frac{V(y)}{E(y)^2} - \frac{2C(x, y)}{E(x)E(y)}\right).$$

Clearly, both of these formulas simplify somewhat when x and y are uncorrelated.

APPLYING THE FORMULAS

In applying the formulas described above, the Committee found it necessary to adopt the following assumptions.

1. Both x and y have normal distributions.
2. The interval estimates for x and y represent 90 percent confidence intervals.
3. The midpoints of the ranges estimate the expected values for the variable.
4. The product and quotient of x and y create distributions that can be reasonably approximated by the normal distribution.
5. x and y are uncorrelated (unless stated otherwise).

The application of these formulas can be illustrated with an example from Chapter 7. The benefits of chlorobenzilate to the Florida IPM program were estimated in Chapter 7 to range from \$0 to \$3 million/year. The non-IPM benefits to Florida citrus growers were estimated to fall between \$0.6 and \$6.6 million annually.

What is the appropriate interval for the sum of these two benefits? In accordance with the above-mentioned assumptions, we can restate, say, the non-IPM benefits as equalling \$3.6 million (± \$3.0 million). The upper limit for the 90 percent confidence interval is presumed to be \$6.6 million in this instance. Thus, \$6.6 million = \$3.6 million + $1.64s_{\bar{x}}$, where $s_{\bar{x}}$ represents the estimated standard deviation around the estimated mean value for the non-IPM benefits. This equation clearly implies that the variance around the estimated mean is $s_{\bar{x}}^2 = \$3.33 \times 10^{12}$. Similar reasoning applied to the IPM benefit estimates yields an estimated variance of $\$8.31 \times 10^{11}$. The square root of the sum of these variances provides a correct estimate of the standard deviation around the sum of the mean values for the two variables, namely $s_{x+y} = \$2.04$ million. Thus, the sum of the midpoints of the two benefit measures yields an estimate of the aggregate benefits in Florida equal to \$5.1 million (±[1.64][\$2.04 million] = \$3.35 million). Alternatively, the aggregate Florida benefits are estimated to range from \$1.75 to \$8.45 million.

It is interesting to note that this estimated range is quite different from the one obtained from simple additions of the lower and upper limits for the individual benefit estimates. This "naive" approach implies a much larger range: \$0.6 to \$9.6 million.

NOTE

1. This discussion draws heavily on Mood *et al.* (1974).

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APPENDIX G

List of Abbreviations Used in This Work

BFSD	Benefits and Field Studies Division, OPP, U.S. EPA
CAG	Carcinogen Assessment Group, U.S. EPA
CAI	Carcinogenic Activity Indicator
CEDM	Committee on Environmental Decision Making, NRC
DBCD	Dibromochloropropane
EDF	Environmental Defense Fund
EPA	U.S. Environmental Protection Agency
FDA	U.S. Food and Drug Administration
FEA	U.S. Federal Energy Administration
FEPCA	Federal Environmental Pesticide Control Act of 1972
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act of 1947
HED	Hazard Evaluation Division, OPP, U.S. EPA
IPM	Integrated Pest Management
IRDC	International Research and Development Corporation
IRLG	Interagency Regulatory Liaison Group
MC	Material costs
NCI	National Cancer Institute
NLM	National Library of Medicine
NRC	National Research Council
OC	"Other" costs
OPP	Office of Pesticide Programs, U.S. EPA
PBA	Preliminary benefit assessment
PC	Pest control costs

PCRC	Pesticide Chemical Review Committee, U.S. EPA
PD	Position document
PEP	Preliminary exposure profile
PEAP	(The Committee on) Prototype Explicit Analyses for Pesticides, NRC
RPAR	Rebuttable Presumption Against Registration
SAP	Scientific Advisory Panel, to OPP, U.S. EPA
S-PBA	Supplement to the PBA
SPRD	Special Pesticide Review Division, OPP, U.S. EPA
SCR	Suspect Chemicals Review program
USDA	U.S. Department of Agriculture
USDA-ATR	USDA assessment team report